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**WORKS NOT INCLUDED IN THESE
VOLUMES**

PHYSIOLOGY OF MAN—Five Volumes of about 500 pages each, 1866–1874. Second Edition, 1875. Volumes IV and V are out of print.

MANUAL OF CHEMICAL EXAMINATION OF THE URINE IN DISEASE, pp. 76, 1870. Sixth Edition, 1884.

TEXT-BOOK OF HUMAN PHYSIOLOGY, pp. 978, 1871. Fourth Edition, 1888.



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COLLECTED ESSAYS AND ARTICLES ON PHYSIOLOGY AND MEDICINE

BY

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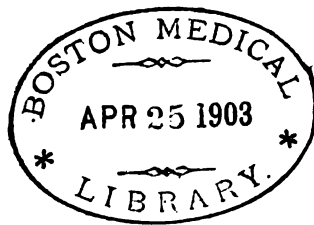
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By AUSTIN FLINT



P R E F A C E

AFTER nearly a half-century of somewhat active and varied literary work, I have collected and printed what is contained in these two volumes, as an offering to those to whom I am bound by ties of relationship or friendship. In effect, I have omitted no article that has been published under my name, however much it may have seemed to me out of place in a collection made up chiefly of serious essays on professional topics. This collection begins, indeed, with a paper written in 1855, and it includes a few articles published in a periodical for young people. It contains, therefore, everything I have written for publication and signed, with the exception of one signed review, one or two biographical memoirs and a very few short articles relating to professional controversies which happily have long since disappeared. It does not include, however, the "Physiology of Man," in five volumes, "Text-Book of Human Physiology" and "Manual of Chemical Examination of the Urine in Disease."

I trust that it may not appear to those for whom these volumes are intended, that it would have been better if I had deferred their publication and left it to be done by others, if at all. With no intention or desire to deprecate criticism, I simply say that they could not have appeared in their present form unless the collection, arrangement and revision had been made by myself; and I feel that the burden of publication should be borne by me and not left as a legacy.

I have revised all the articles very carefully, but not more freely than is frequently done in the correction of first proofs. While I have eliminated some verbal redundancies and attempted to correct what seemed to me noticeable inelegancies of expression, especially in the earlier writings, I have not changed the sense of any one article, paragraph or sentence. It is proper that I should make this statement for the reason that in a short analysis of some of the articles, which is to follow, there will be involved questions of priority of experiment, observation and publication.

It was my intention to arrange the articles chronologically; but I have deviated from this order in putting together those on purely physiological and medical subjects, following them with the miscellaneous writings. I have also grouped a few articles on similar topics, especially when they represented series of experiments or observations. In some few instances there have been partial repetitions, the same facts or arguments being used in different relations. With these exceptions the chronological order has been preserved; and the date and place of publication have been given in every instance, so that a claim of priority of publication may be verified by any one interested sufficiently to refer to the original.

The text-books on physiology of fifty years ago were not often the work of practical physiologists; and in attempts to present fairly the best opinions on the questions considered, not infrequently opposite views of observers were given, leaving to the reader the responsibility of selection. It was seldom, indeed, especially in works published in the English language, that matters in doubt or dispute were discussed by authors practically familiar with methods of physiological experimentation.

In 1857, the date of publication of the article on "Phenomena of the Capillary Circulation," there were writers

of authority who taught that the blood moved in the capillary vessels in obedience to what was called the "capillary power," an attractive force exerted by the tissues on the nutritive constituents of the circulating fluid. In my inaugural thesis (1857) I attempted to describe the varied phenomena observed in studying the capillary circulation under the microscope. In the course of these observations I was fortunate enough to hit upon a method of suppressing cutaneous respiration in the frog by covering the surface with a coating of collodion, which enabled me to study the immediate effects of asphyxia on the capillary circulation by direct examination. These were the first microscopical observations of the arrest of capillary circulation following suppression of the respiratory function; and they seem to me to be important even now, as showing that blood deficient in oxygen can not circulate freely in the capillaries, the obstruction being in the systemic vessels and not in the lungs. While the demonstration was original, the theory was not new. Dr. John Reid, of Edinburgh, advanced the same view in 1841. He showed that the arterial blood-pressure in an asphyxiated dog was much increased, while the pressure in a corresponding vein was proportionally diminished as the asphyxia proceeded to the stage of insensibility.

In 1861 I made a number of experiments on the roots of the spinal nerves and confirmed the observations of Magendie, made in 1839, in which it was shown that the anterior roots possessed a slight sensibility derived from recurrent fibres from the posterior roots, concerning which there had been differences of opinion. These were the first observations of the kind made in this country.

In 1868 I had an opportunity of examining what purported to be an exact reprint of the celebrated "Idea of a New Anatomy of the Brain," by Sir Charles Bell, the

then reputed discoverer of the distinct properties and functions of the two roots of the spinal nerves. This pamphlet was printed for private distribution only and was practically inaccessible. I published in that year an extended review of the claims of Bell and of Magendie to this important discovery and corrected an error almost universal in the literature, including, even, the works of French authors, attributing the discovery to Bell. I make mention here of this publication for the reason that it led writers generally, for the first time, to do justice to the claims of Magendie. The article was followed by a republication of Sir Charles Bell's pamphlet in the "Journal of Physiology," in 1869; and I had the satisfaction of seeing that the reprint which I had used was accurate and that my conclusions were justified.

In the articles on the action of the heart and on respiration, published in 1861, 1874, 1877 and 1880, are records of experiments which justify a claim of priority in the description and explanation of certain phenomena observed later by others and now universally adopted by writers on physiology. I had an opportunity, while teaching physiology in the New Orleans School of Medicine, in 1860 and 1861, to experiment on alligators of large size. It is well known that the excised heart of cold-blooded animals will continue to beat for a considerable time. I demonstrated that the heart, when filled with blood, the valves between the cavities having been cut away, will beat powerfully and with regular rhythm; while the pulsations are more rapid, feeble and irregular when the cavities are empty. I also showed that the pulsations are relatively rapid and feeble when the cavities are filled with water instead of blood. I made an application of the phenomena observed to the rapid and feeble action of the heart in the reaction from hemorrhage and in anemia. The recent "perfusion experiments," made chiefly

on the heart of the frog, are to a certain extent elaborations of these observations. Systematic perfusion experiments are said to have been begun by Merunowicz, in Ludwig's laboratory, in 1875. They were repeated, with improved methods, by Cyon and the phenomena observed are now the subject of extended investigation.

In this series of experiments I showed that while curara usually paralyzes the inhibitory nerves of the heart, as well as the general motor system, in alligators these nerves are not affected by the poison. Bernard had shown this to be the case in birds. In addition to the observations on alligators I showed that in dogs enfeebled by loss of blood inhibition of the heart is but slightly affected by curara. I reasoned from this that these nerves are "protected from disturbing influences, like the action of poisons, to a greater degree than others."

The experiments on respiration, published in 1861, led me to think that the "respiratory sense" had its origin in the general system and was due to want of oxygen. I expressed the same opinion in an address on the "Mechanism of Reflex Nervous Action in Normal Respiration," published in 1874.

In 1877, when I extended my observations on the "respiratory sense," or the starting point of the impulses which give rise to the movements of inspiration, opinions as to the action of the respiratory centre in the bulb were varied and conflicting. Rosenthal (1862) and Pflüger (1868), subsequently to my experiments of 1861, had shown that the respiratory sense was due to a general deficiency of oxygen in the system, having noted dyspnea in animals made to breathe pure nitrogen or hydrogen. Kussmaul and Tenner (before 1858), having noted dyspnea after ligation of the carotids, extended previous observations and referred the convulsions observed in suffocation and after profuse hemorrhage to a deficiency in oxygen in the brain and in the bulb. They described the

so-called "convulsions of anemia"; and some physiologists assumed the existence of a "convulsion-centre" in the bulb. As early as 1839 John Reid wrote that the respiratory movements were due to the action of black blood in the bulb. In 1841 Volkmann attributed the respiratory movements to the stimulation of carbonic acid in every part of the body. Direct and conclusive experiments, however, showing the effects of cutting off the blood-supply from the brain and bulb, contrasted with those observed after cutting off the supply from the trunk and lower extremities, were wanting. In my experiments, first published in 1877, and discussed fully, with a review of the literature, in an article entitled "Is the Action of the Medulla Oblongata in Normal Respiration Reflex?" published in 1880, I showed that after arresting the respiratory movements in animals by supplying air in abundance to the lungs in artificial respiration, respiratory efforts began, although artificial respiration was continued, when the vessels given off from the arch of the aorta were tied; and that no respiratory efforts were made when the aorta was tied below the arch and arterial blood was allowed to circulate in the head and anterior extremities. I believe these to be the first experiments demonstrating positively the effects of depriving the respiratory centre of oxygen. The views resulting from these observations are now universally accepted.

Eighteen hundred and sixty-two is the date of the publication of what appears in these volumes as Article IX., on a "New Excretory Function of the Liver." This article was published in French in 1868. In 1869 it received an "honorable mention" with a "recompense" of 1,500 francs from the Institute of France (Académie des Sciences), Concours Monthyon (médecine et chirurgie), being second to the essay by Villemin, on the specific character and inoculability of tuberculosis, the most important

work in medicine since the discovery of vaccination, which received the Monthyon prize for that year. In 1876 I gave an abstract of my work in an address before the International Medical Congress held in Philadelphia. Another abstract, with a review of the literature since 1862, appeared in the "New York Medical Journal," in 1877.

I mention all of these publications in this place, for the reason that in 1896 an article appeared in Hoppe-Seyler's "Zeitschrift," in which most of my experiments and physiological deductions were published as original by two workers in Schroeder's Pharmacological Institute in Heidelberg.

In my article of 1862 I described a new substance extracted from normal feces, which I called stercorin. I showed that this substance was excrementitious and that it resulted from a change of the cholesterin of the bile in its passage through the small intestine, incident to the process of intestinal digestion; that cholesterin was probably a catabolic product of nerve-tissue; that in certain extensive structural diseases of the liver, the proportion of cholesterin in the blood was largely increased, constituting a condition which I called cholesteremia; and that this might account for theretofore unexplained grave nervous symptoms.

The chemists who claimed to have discovered a new substance in the feces called it "koprosterin." They obtained it by practically the same process employed by me for the extraction of stercorin, in 1862. The only variations which saved their method from being identical with the process employed by me were the use of Soxhlet's extraction-apparatus, not known in 1862, by which the ethereal extracts were made more rapidly, and the removal of fats by saponification with sodium alcoholate instead of potassium hydrate.

In 1897, in the Address on Medicine at the semicentennial anniversary of the American Medical Association,

I gave an account of new experiments in which I extracted stercorin by my original process and by this process as modified in 1896. I also compared the two products with a specimen of stercorin extracted in 1862, which I had fortunately preserved, verifying the empiric formula for each. I found the three products to be identical as to formula, reactions and form of crystals.

Later in 1897 I sent these facts to Hoppe-Seyler's "Zeitschrift," with a reclamation of priority, which were published in German in August of the same year. The discoverers of "koprosterin" denied my claim of the identity of their product with stercorin, basing this denial on a statement made by me in 1862, that stercorin fused at 36° C. "Koprosterin" fuses at 95° – 96° . In 1862 I regarded stercorin as probably identical with a substance which had been extracted in minute quantity from the serum of the blood, by Boudet, called séroline; and I quoted Lehmann as giving 36° as its fusing point. I do not remember, after an interval of forty years, that I attempted to take the fusing point of the stercorin which I obtained from feces.

In this brief analysis I have simply recited facts which I trust some may take the trouble to verify by referring to the articles themselves; and I have no desire to add what can be regarded as in any degree polemic. Assuming a familiarity on the part of the chemists referred to with the literature—which was not denied—I venture only to suggest, as a possible reason why the pathological as well as the physiological ideas as to the relations of stercorin were not appropriated, that workers in pure chemistry can hardly be expected to appreciate the importance of such researches in their applications to practical medicine.

At the time the article "On the Organic Nitrogenous Principles of the Body with a New Method for their Esti-

mation in the Blood" was published (1863), all the analyses of the blood to be found in works on physiology gave estimates of dried albumin, fibrin and corpuscles. The "new method" described in this article refers chiefly to estimates of albumin and fibrin. Physiological chemists, among whom may be mentioned Dumas, Denis, Figuier, Becquerel and Rodier, Schmidt, and Zimmermann, had attempted to estimate the corpuscles in their moist, or natural condition. In my analyses for organic nitrogenous matters I obtained the proportions of moist albumin and fibrin; but physiologists now recognize, instead of albumin and fibrin, a number of proteids in the blood-plasma that had not been described in 1863. I succeeded, employing a method adapted from Figuier, in estimating, with fair accuracy, the corpuscles in their normal condition. Many attempts to do this had been made, by processes very complex and uncertain. Nearly all works on physiology now give the proportion of moist corpuscles, which closely corresponds with my estimates; and the method which I employed was so simple and easy of application that it could be made use of in hospital or private practice. Of late years, however, apparatus for blood-counting has superseded chemical analysis in clinical work.

The remarkable discovery by Bernard, published in 1848, of what he called the sugar-producing function of the liver was received with much enthusiasm; and his remarkable experiments were extensively repeated and frequently used as demonstrations in the teaching of physiology. A few years later, Pavy claimed to have demonstrated that neither the liver nor the blood of the veins between the liver and the heart contains sugar during life; and that the sugar found by Bernard in the liver and in the blood of the hepatic veins was the result of post-mortem change of an amyloid substance. This latter view

found many adherents, particularly in England and Germany; so that in 1869 the question was unsettled.

In 1869 I published an account of experiments "undertaken for the purpose of reconciling some of the discordant observations on the glycogenic function of the liver." These experiments, so far as I know, were the first made with this object. In 1857 the description by Bernard of a substance in the liver, called glycogen, which is gradually changed into sugar by a ferment and is carried away as sugar by the hepatic veins, seemed to complete the discovery of the glycogenic function. In my experiments I attempted the analysis of the substance of the liver in a condition as nearly as possible approaching that of the organ actually in the living body. I opened the abdomen rapidly and cut a portion of the liver, previously rinsed in warm water, into boiling water, the operation lasting but ten seconds. I found no sugar in the liver, but the blood of the hepatic veins, taken from the same dog, contained sugar. From these experiments I concluded that during life the liver contains no sugar, thus verifying the results obtained by Pavy; but that sugar resulting from a transformation of glycogen, as fast as it is formed, is washed out by the blood-current and appears in the blood of the hepatic veins, thus confirming the results obtained by Bernard. My experiments seemed to harmonize the apparently discordant observations of these two physiologists. Since that time it has been the generally received opinion that the liver stores up the products of digestion of the carbohydrates in the form of glycogen, and, in the carnivora at least, produces glycogen, probably from the proteids; and that glycogen is gradually changed into sugar which is carried away in the blood of the hepatic veins, where it always exists during life. In the experiments recorded in this article portions of the liver were taken from living animals and analyzed for sugar much more rapidly than in any previous ob-

servations with which I am acquainted. These experiments were repeated and somewhat extended by Lusk in 1870.

The ideas in regard to the storing up of the carbohydrates of food in the liver in the form of glycogen and their gradual discharge into the blood in the form of sugar, which these and other observations led me to entertain, prompted me to make studies of the relations of diet to diabetes mellitus, the results of which appear in Articles XV., XVI. and XVII., published in 1884 and 1887.

In 1870 my interest in physical training and athletics led me to witness the close of an effort by a professional pedestrian to walk a hundred miles in twenty-two consecutive hours. By a mere chance I was able to procure all the urine said to have been passed during that period. The attempted feat of endurance was accomplished; and my examination of the urine seemed to show that the unusual muscular effort largely increased the elimination of nitrogen by the kidneys. This result encouraged me to make an attempt to settle the disputed question of the influence of muscular work on the elimination of nitrogen, by a carefully prepared and much more elaborate series of investigations on the same person in an attempt to walk four hundred miles in five consecutive days. The details of these observations, made in the fall of 1870, are embodied in Articles XVIII., XIX. and XX. The results were definite and, as it seemed to me, conclusive. I compared the outgo with the income of nitrogen for three periods of five days each, including the five days of the walk.

The most important of the conclusions related to the elimination of nitrogen and its proportion to the nitrogen of the food. For the five days of the walk, I found 154 parts of nitrogen discharged for every 100 parts of nitrogen of food, against 93 parts, for the five days before the

walk, and 85 parts, for the five days after the walk. The investigations which formed the basis of these articles involved much labor, and they are by far the most extensive ever made on the questions considered. However, in 1876 a similar series of observations was made by Dr. Pavy, of London, upon the same person, in a walk of six consecutive days. The general results of these experiments confirmed my own, obtained in 1870; although my conclusions were not accepted, on theoretical grounds.

A careful study of the observations by Dr. Pavy and others led me to publish, in 1877, the essay entitled "Source of Muscular Power," in which I embodied my own investigations, made in 1870, the results of Dr. Pavy's investigations, made in 1876, with a discussion of experiments by other physiologists, made on a smaller scale. Since this publication it has appeared that certain quoted estimates—at the best of doubtful accuracy—used in my calculations, probably were incorrect; but the possible errors involved do not materially affect the general conclusions. Quoting from this essay:

"I feel that I am justified in claiming priority in the method of investigating the influence of exercise upon the excretion of nitrogen by comparing the nitrogen eliminated with the nitrogen of food."

As my experimental data seemed opposed to the views of Fick and Wislicenus, which were then quite generally accepted, the observations and conclusions of Oppenheim, made in 1880, are of interest. Oppenheim concludes that muscular work, when not carried to the extent of producing shortness of breath or when moderate and extending over a considerable length of time, does not increase the elimination of nitrogen; but that even less work, when violent and attended with shortness of breath, increases the discharge of nitrogen. In other words, when the increased elimination of carbon dioxide, due to muscular work, has reached its limit, the additional work is repre-

sented by an increased elimination of nitrogen. An acceptance of this proposition would go far to harmonize the results obtained by different experimenters.

Without further discussion I may say that recent advances in knowledge of the phenomena of nutrition and catabolism do not seem to have impaired, in any important degree, the value of my experiments and conclusions made thirty-two years ago.

The researches which formed the basis of the articles upon the influence of muscular work on the elimination of nitrogen and the essay on the source of muscular power naturally led to a study of animal heat and the applications of the theories of calorification to fever and its rational treatment. In discussing the source of muscular power I made use of the estimate by Senator, of the probable production of four heat-units per hour per pound of body-weight; and the same estimate was adopted in the article, "Experiments and Reflections on Animal Heat," published in 1879. With this estimate—which I regarded as not entirely reliable—it seemed impossible to account for the heat thus assumed to be actually produced and either used or lost by radiation, by the heat-value of food. Even with the estimate, made by the indirect method, of two and a half heat-units per pound per hour, it was difficult to account for the heat produced, by the heat-value of the processes usually regarded as involved in calorification.

Assuming that the total heat produced in the body, deducting the loss by heat-dissipation, is used to maintain the animal temperature and to accomplish work, the elements in the problem of its expenditure are discouragingly uncertain as regards estimates of the quantities converted into force to maintain circulation and respiration and to accomplish general muscular work. The most important element in this problem, however, is the estimation of the actual quantity of heat produced per pound of body-weight

per hour; and a fairly accurate estimate of this would render calculations of the proportion lost, the proportion used as force and to maintain the body temperature comparatively unimportant in ascertaining the sources of heat-production and muscular power; assuming, as we must, the validity of the law of the correlation and conservation of forces. But with the lowest estimates of heat expended as force, it is difficult, if not impossible to account for it by the heat-value of food or tissue consumed, represented by the excreta, assuming anything near accuracy in these measurements. To solve the problem, even approximately, it is necessary to find sources of heat which will much more than account for the work, reduced back from force-units to heat-units, the maintenance of body-heat and the loss by heat-dissipation.

The difficulties that I have indicated in a measure account for the indefinite, not to say obscure manner in which the subject of animal heat and force is treated in nearly all modern systematic treatises on physiology. In general terms, it may be said that the indirect method of estimating heat-production is to calculate the heat-value of oxygen taken in and correct this by comparing it with the heat-value represented by oxidized matters discharged. This has been found to correspond fairly well with the calculated heat-value of food. Such a calculation, however, almost begs the question; it simply indicates what should be the heat-production and assumes that the heat-production is what the calculations show that it should be. The strictly logical process is the direct method, using the calorimeter, and measuring, if possible, the heat actually produced. By the indirect method, the calculated heat-production about equals the calculated heat-value of food, with the body in a condition of physiological equilibrium; but the food accounts for only about $62\frac{1}{2}$ per cent. of the heat actually produced, calculated by the direct method. With the very large elements of uncertainty in

the reduction of the force used in circulation and respiration and in general muscular work to heat-units, the question of heat and force-production in the body seems as far from a satisfactory solution to-day as it was before 1879.

Although Lavoisier and Laplace, in 1780 and 1785, had attributed heat-production to oxidation of carbon and hydrogen, it had never been demonstrated, before my experiments published in 1879, that oxygen actually unites in the body with hydrogen to form water. The heat-value of such oxidation is very great; and this, added to the heat represented by the carbon dioxide, urea, etc., eliminated, would much more than account for the heat actually produced and used either as heat or as force, making the calculations of heat produced, either by the direct or by the indirect method. The increase in the production of water due to increased muscular work also would account for the necessary increase in the production of heat to supply the force.

I think I was the first to demonstrate positively by experiments, some of which were made on my own person, that under conditions, at least, when oxidation represented by carbon dioxide and nitrogenous excretions is not sufficient to supply the heat required, water is produced in the body, as is shown by a considerable excess of water discharged over and above the water taken in, without loss of water by the liquids and tissues of the organism. I could thus account, also, for the oxygen of the respired air lost and not represented in carbon dioxide and other excreta.

At the ninth session of the International Medical Congress, held in Washington in 1887, addresses were made in general session by representatives of Great Britain, France, Austria, Germany, Italy and the United States. I was honored with the appointment to deliver the address in behalf of the United States; and I chose the sub-

ject of "Fever." In this address I endeavored to apply my studies in animal heat to the mechanism and rational treatment of fever, especially in the way of supplying material to feed the fever and save the tissues until the disease should have run its self-limited course, restricting, also, the destruction and degenerations of tissue by reducing temperature. I took the ground that in certain cases it became necessary to "feed the fever" with alcohol.

There has been, is at the present time and probably will be far into the future, violent and acrimonious discussion as to the fate of alcohol taken into the body. The main question now agitated is whether or not alcohol, taken in quantity not sufficient to produce intoxication, is oxidized and serves as food or, if not directly as food, as an agent restricting the waste of tissue. A controversy between the laity, opposed on moral grounds to the use of alcohol, and scientific observers not practically familiar with disease and its treatment but relying on studies of the changes which alcohol undergoes in the healthy organism, is not likely to promote a scientific solution of the question involved. While it may be that in a healthy person, adequately nourished, alcohol is not useful, even if not actually harmful, and that it can not contribute, except momentarily, to mental or physical power and endurance, in its judicious and careful therapeutic administration, in many diseases, it is often of great value. I therefore adhere to the views embodied in the two articles on fever and in the article "On Some of the Therapeutic Uses of Alcohol," published in 1887.

It is calculated that 10 grains of absolute alcohol, when oxidized, will produce 23 heat-units; and one ounce, weighing about 384 grains, is equal to about 883 heat-units. In fever alcohol administered in certain quantity is not eliminated as alcohol; it does not intoxicate and, as it seems, it must be oxidized. Thus admin-

istered it does not increase pyrexia; and if oxidized, it must save tissue and moderate degenerations. If these statements are true, alcohol can not properly be eliminated from therapeutics any more than morphin or strychnin.

While I have thought it well, for the benefit of those who may be led to read some of the articles here republished, to give, in a brief analysis, a rather more extended account of what is contained in these volumes than is to be found in the Table of Contents, I have not intended to refer to individual articles unless they presented some claim to original investigation or to unusual methods of treatment of the subjects considered. In the three articles on examination of urine I insisted on the importance of examinations in all cases of application for life insurance, which was rarely done at the time I became a medical examiner for a large company, in 1871. An experience of fifteen years in such work confirmed me in this judgment. I endeavored, also, to popularize in the profession urinary examinations by the general practitioner, by presenting rapid and easy methods sufficiently accurate for ordinary clinical purposes.

In 1888 I reported a case, in Article XXXII., of sciatica treated, with very prompt relief, with doses of anti-febrin much larger than ever used before.

I may also refer briefly to a "Tonic Formula" (Article XXXIII.), which has been largely used since the publication of this article in 1889. In calculating this formula I endeavored to make a preparation containing the inorganic constituents of the blood in about the normal proportions, with an excess of iron and of sodium chloride, to be used as a remedy in certain cases in which it seemed to me that patients were suffering from deficiency in saline matters as well as corpuscles. My own experience with

the "Saline and Chalybeate Tonic" has been quite satisfactory; and I have lately seen an imitation of the formula recommended for the purpose I have indicated.

The so-called "Frenchy" murder trial, in 1891, excited at the time great professional and popular interest, on account of the peculiar atrocity of the crime, the savage character and history of the accused and the very unusual nature of the expert testimony. The evidence in this case was entirely circumstantial; and there is now much difference of opinion in regard to the justice of the verdict. This case was again brought to public notice by the release of the prisoner after eleven years of confinement under a life sentence for murder in the second degree, part of the time in the Asylum for Insane Criminals. The very last article of this collection gives a brief retrospect of the case, written on the occasion of the action of the Governor of the State of New York.

The verdict of the jury rested practically on testimony as to recognizable differences between the contents of the small and of the large intestine, small portions of which were found about the person of the victim and the person of the accused, including matters taken from beneath the finger nails. "The evidence which convicted the prisoner was that the various specimens examined by the experts for the people presented blood mixed with matters which must have come from the small intestine, and which by no reasonable theory, could be on the prisoner's clothing and person unless they came from the body of the murdered woman. It is this point in the case which, so far as I know, is without precedent and is of peculiar medico-legal interest."

It is to be regretted that a full report of this case has never been published and that my own testimony is all that has appeared. So far as expert work is concerned, the case is unique.

Late in 1892 I began to use bismuth subgallate in so-called functional dyspepsia attended with gastric and intestinal flatulence. I was led to the use of this remedy by seeing it recommended for the diarrhea of children, acting as a disinfectant. I think I was the first to administer it in ordinary digestive disturbances. It is now very extensively prescribed, and the general experience in regard to its value as an antifermentative is in accord with my own.

The case of "Filaria" with chyluria (Article XXXVI.), reported in 1895, is the first on record in which methylene blue was employed with the view of destroying this remarkable nocturnal parasite. I advised this remedy in the case reported, reasoning from my experience in its action on the plasmodium malarix. It was suggested in this article that there was a "possibility of benefit from methylene blue in the treatment of other diseases due to the filaria, such as chylous collections in the peritoneal cavity and in the cavity of the tunica vaginalis testis, hematuria and elephantiasis."

In 1867, at the request of the then Commissioners of Public Charities and Correction of the City of New York, I made an examination of the food supplies and methods of cooking and serving in Bellevue Hospital and in the other hospitals, prisons, etc., under their charge. This resulted in the recommendation of the dietaries embodied in Article XXXVII. It is almost unnecessary to say that for many years, the sick poor, the pauper insane, prisoners and others, including infants and children, under the care of the City and State have been subject to the vicissitudes of politics. They suffer, on the one hand, from the ignorance or indifference of administration, and on the other, from well-meant efforts of dietetists to reduce nutritive supply to the calculated requirements of nitrogen

and carbon. It is fair to say that the dietaries suggested were for a time carried out as fully as possible under the then existing methods of purchase of supplies and of appointment of subordinate officers; but the many, and sometimes revolutionary changes in administration, that have occurred since 1867, have led to such modifications in these dietaries that their original character has long since disappeared. I take this opportunity, however, again to express my confidence in dietaries constructed on physiological rather than on purely chemical principles applied to metabolism; a belief which I think is shared by physicians familiar with disorders in general nutrition so often seen in private practice as well as in hospitals, asylums and prisons.

I also prepared dietaries for the State Hospitals for the Insane, in 1893, the population of which considerably exceeded twenty thousand. These dietaries were placed on trial for one year. They were then revised in accordance with suggestions and recommendations made by the Superintendents of the different hospitals. The revised report is republished as Article XXXVIII.

In 1898 there was a change in the personnel of the State Commission in Lunacy; and the dietaries in operation since 1894 were superseded on the ground of economy. I can not question the wisdom of this change, for lack of information in regard to the experience with the new schedules; although very elaborate tables showing the calculated nutritive requirements were published in 1899 and 1900, in which it appeared that these requirements could be adequately met by the calculated nutritive values of supplies less than those in use. Still another change occurred, in December, 1900, when the President of the Commission, appointed in 1898, was removed by the Governor. The dietaries were again more or less modified under the new administration; but I have little or no information as to the nature of these changes.

In 1895, at the request of the Comptroller of the State of New York, I prepared schedules of diet for the various State charitable and reformatory institutions reporting to the Comptroller's Office. These were made on the same general lines as those of the dietaries for the State hospitals, but with certain modifications that are indicated in Article XXXIX. These dietaries, however, were never put into operation, and they are now published for the first time.

I was appointed by the Governor of the State of New York, in 1894, the medical member of a commission of three to investigate the administration of the New York State Reformatory at Elmira, in view of certain charges brought against the General Superintendent. I was the joint author, with the Hon. Israel T. Deyo, of the majority report of this commission, which was adopted by the Governor. This report is not republished in these volumes for the reason that I was not its sole author; but I am glad to have the opportunity of putting myself again on record as approving the reformatory system, especially as it was carried out at Elmira. Article LIX., on the "Scientific Treatment of Crime and Criminals," and Article LX., "The Pain of Death," embody most of the features of this report that are of interest to the medical profession and to criminologists.

I am also more than ready to go on record as opposed to capital punishment. My views on this question—one of great importance to our social system—are contained in the address on "The Pain of Death," before the "Quill Club," made in 1897.

What I have just written completes the analysis of the strictly scientific essays and articles. In addition to these are twenty-one magazine articles, which have appeared in various periodicals between 1866 and 1901, including

two ("Gymnastics" and "Pugilism") published in the "American Cyclopædia," in 1874 and 1875. In these articles I attempted the difficult task of popularizing certain scientific subjects. Many of the titles are not my own but were suggested by editors. I do not feel competent to decide whether or not my efforts to clothe scientific questions in popular language and style have been successful. Articles LIV., LV. and LVI., however, are more serious than some of those classed as "Miscellaneous." They were published in "The Forum" in 1888, 1889 and 1891 and are devoted mainly to bacteriology and its bearing on the recent remarkable progress in medicine and surgery. It is gratifying to see that many of the predictions which I ventured to make at the time these articles were written, when the bacterial theories of disease were in their infancy, have since been realized. Studies in bacteriology, dating from the discovery of the tubercle bacillus by Koch, in 1882, excited much popular as well as scientific interest; and "The Forum" was one of the first of the magazines devoted to general literature to publish articles on this subject.

The rather formidable list following the name on the title page would, perhaps, be out of place, except as representing a personal professional history in volumes which include all my literary work up to the present date.

NEW YORK, *November, 1902.*

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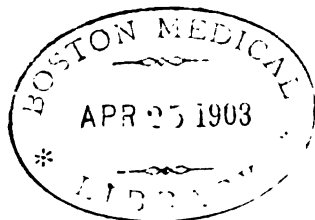
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I

AN ANALYSIS OF ONE HUNDRED AND SIX CASES OF PARONYCHIA

Published in the "Buffalo Medical Journal" for October, 1855.

PARONYCHIA BENIGNA

THE private records of Dr. F. H. Hamilton contain eighty-one cases of paronychia benigna.

In all these cases the sex has been noted, and the proportion of females to males is nearly two to one, there being fifty-three females and twenty-eight males. In considering the occupation of these patients and, as far as could be ascertained, the causes which operated to produce the disease, in the great majority of cases it was found that the occupation involved manual labor; and where the occupation was noted as the cause of the disease, it was most frequently an occupation in which females are generally engaged. In the male patients, the cause was generally a bruise or slight injury to one of the fingers and not the occupation. As feminine duties frequently cause paronychia and accidental injuries are the most frequent causes in the male subject, it is not surprising to find a larger proportion of cases occurring in females.

In sixty-one cases the hand affected with the paronychia was designated.

Of these cases forty-two occurred on the right hand and nineteen on the left; showing that the right hand, being more used and more subject to accidental injuries, is much more liable to this affection.

In seventy-five cases the diseased finger was designated. The thumb and first finger, which are most used, were affected in the greatest proportion of cases and appeared to be about equally liable to the disease. The thumb was the seat of the affection in thirty-two cases and the first

finger in twenty-seven. The second finger was next in order, being affected in ten cases. There were but two cases affecting the third finger; one affecting the fourth finger; two affecting the first, second and third; and one affecting the second and third. The last three cases were of the first variety, onychia cutanea. One of them was caused by pricking the finger in sewing. This was very trivial and got well spontaneously. The other two were caused by suppressed menses and were soon cured by nitrate of silver and poultices. Thus, not only the hand, but the fingers which are most used are most liable to paronychia.

In sixty-three cases the ages of the patients were noted.

I found but three cases under fifteen years of age. One of these patients was two years of age, another three years and another eleven years. There were thirty-eight cases from fifteen years to thirty; nineteen from thirty to forty-five; two from forty-five to sixty, (one aged forty-eight and the other fifty); and one from sixty to seventy-five, (aged sixty-one).

According to these facts, paronychia is rarely met with in patients under fifteen years of age or over forty-five; although it may occur at the age of two or three years or as late as sixty-one. The favorite age appears to be from fifteen to thirty, at which period nearly two-thirds of the cases, where the age was recorded, were observed. It is by no means infrequent, however, from thirty to forty-five, at which period nearly one-third of the cases have occurred.

In sixty-three cases the occupation of the patient was recorded.

In all but seven of these cases, the patients were engaged in occupations requiring considerable manual labor. These seven exceptions were a clerk, a clergyman, a doctor, a student of medicine, a female teacher and two children at school. The remaining fifty-seven were mechanics, laborers or housemaids. Of these there were twenty-three housemaids, five housewives, five seamstresses and two laundresses. Of the males there were five shoemakers, four laborers, two sailors and two blacksmiths.

By far the largest number of cases of any one occupation was the number of housemaids, twenty-three out of

sixty-three, more than one-third of the entire number, and nearly five times the number of cases of any other occupation, five being the next highest number.

In fifty-one cases the probable cause of the affection was recorded.

Under this head I find the occupation recorded as the cause in twenty-three cases. Of these, nine were accustomed to housework, scrubbing, etc. One of the patients, a shoemaker, says that shoemakers are peculiarly liable to paronychia from turning boots inside out. A similar statement was made by another patient, who said that lathers and plasterers were liable to it, from driving small nails and frequently bruising their fingers.

Five cases were caused by bad health; two cases were the result of slight wounds; two cases were caused by suppressed menses. These were of the first variety, paronychia cutanea, and were treated with nitrate of silver and poultices. One case, a boy three years old, was caused by his being deprived of meat under the impression that he would thus avoid the cholera. He had been accustomed to meat diet and ordinarily was healthy; but now he has a paronychia and cankers in his mouth and nose. A clergyman brought on a felon by rowing a boat; a school girl, by practicing on the piano; and a housemaid, by washing dishes. One case occurred after an attack of ship fever. Another case, a seamstress, occurred in a patient of a scrofulous diathesis who had an anal fistula.

From the foregoing facts it is seen that the causes of paronychia are various. The most frequent causes, however, are exposure of the hands to hot water, as in washing dishes, or a slight hurt or bruise. In forty-one cases the causes were of this description. More rarely the cause is general or constitutional. In ten cases the causes were recorded as bad health, ship fever, suppressed menses, etc.

Of the entire number of cases one was not properly a paronychia but was a fungus at the root of the nail; eight were of the first variety, paronychia cutanea; five were of the first and second variety, cutanea and cellulosa; and the remaining sixty-seven were of the second, third and fourth varieties, cellulosa, tendinosa and osteosa. In the case of the fungus at the root of the nail nothing is recorded but

that on the twenty-first day the fungus was the size of a pea.

The cause was recorded as constitutional in three of the five cases, which were of the first and second varieties combined. There was no record, under this head, in the remaining two cases. In three of these cases the treatment was merely the application of nitrate of silver; one case discharged spontaneously on the eighth day, but the inflammation extended to the areolar tissue, pus was formed and it was opened on the fourteenth day; in the remaining case there was no record under the head of treatment. All these cases resulted in perfect cures.

Of the eight cases of the first variety, paronychia cutanea, six were caused by slight injuries and two were dependent upon constitutional causes. Six were treated with nitrate of silver and poultices; one, with poultices only; and one got well spontaneously. One, however, was opened before the nitrate of silver was applied. Four of these cases resulted in perfect cures, one of them, in the loss of the nail, and the remaining three appear to have been lost sight of.

In the sixty-seven cases which were of the second, third and fourth varieties, I shall consider only one feature in the treatment; namely, whether it was opened or not and how long after the onset of the disease before it was opened. The other measures of treatment were so imperfectly recorded that their consideration would be of little value.

In fifty-five cases the results were recorded. Thirty-six resulted in perfect cures; and nineteen, either in loss of part of the finger or in ankylosis.

Of the thirty-six cases twenty-nine were opened; in the remaining seven cases there was no record under this head. In twenty-seven cases pus had been formed. The remaining nine did not suppurate.

Of the twenty-nine cases where the finger was laid open, ten were opened on the seventh day. Eight of these had supplicated and two had not. Seven were opened on the tenth day; three on the fourteenth day; two on the thirteenth day; one on the eighth day; one on the eleventh day; and one on the fifth day. All of these had supplicated. Two were opened on the fourth day, one having supplicated

and one not. One was opened on the third day and one on the second day, neither of them having suppurated.

In the nineteen cases where the cure was imperfect, twelve were opened and in seven there was no record under this head. One was opened on the twenty-eighth day; one on the twentieth day; one on the fifteenth day; one on the fourteenth day; two on the seventh day; and one on the fourth day. In the last case no pus was found. One case discharged spontaneously. This case was treated by an empiric, who was prosecuted and mulcted in damages for not opening the finger. The case resulted in a loss of the entire finger.

From the results of these fifty-five cases it is seen that a perfect cure may be expected in the majority of cases. In the cases which resulted in perfect cures only six out of twenty-nine were opened after the tenth day; seven were opened on the tenth day; ten on the seventh day; and one was opened as early as the second day, before pus had been formed. None were opened later than the fourteenth day. But in the cases where the cure was imperfect, one was not opened at all; seven were opened from the fourteenth to the twenty-eighth day; two only were opened as early as the seventh day, and one on the fourth day.

These facts show the importance of opening the finger at least as early as the tenth day; and it seems, indeed, to be proper to do so as soon as the disease becomes established, even before pus has been formed.

INFLAMMATION OF THE FINGER OF THE SAME CHARACTER AS PARONYCHIA, BUT NOT IN THE LAST PHALANX

Dr. Hamilton recorded eighteen cases which came under this head. In nearly every particular they are the same as paronychia proper; but as the number of these cases is large, it may be as well to consider them by themselves.

As in paronychia, female patients predominate, ten being females and eight males. The age at which they seem to be most liable to the affection is also the same. No case occurred under fifteen years; twelve cases from fifteen to thirty; three from thirty to forty-five; two at thirty-two years; and one at thirty-seven. No cases occurred after the age of thirty-seven.

The right hand was affected in eight out of ten cases, where the hand was noted. Out of thirteen cases the thumb was affected in one case; the first finger in one case; the second finger in six cases; the third finger in five cases; but in no case was the fourth finger affected. Here is a difference from paronychia, where the thumb and first finger were affected in a great majority of cases. I can see no cause for this difference, except, perhaps, that the causes which produce this affection appear to be more purely accidental than in paronychia and not so much due to the occupation of the patient; and that the last phalanges of the thumb and forefinger are most used, not the entire finger and thumb, while the other phalanges of the second and third fingers are, perhaps, more liable to accidental injuries than the first phalanx of the thumb or the first or second phalanges of the forefinger.

Of sixteen cases the first phalanx was affected in four cases; the first and second in one case; the second in five cases; the second and third in one case; and the metacarpophalangeal articulation in five cases. This shows that the first and second phalanges are about equally liable to it; and also the metacarpophalangeal articulation.

As regards the occupation of the patients, it is seen that the same classes of society are affected with this disease as those affected with paronychia. Here, also, housemaids and housewives predominate. Of seventeen cases there were six housemaids, three housewives, two sailors, two stone cutters, one cabinet maker, one male cook, one cooper and one clergyman. The clergyman is the one referred to in the cases of paronychia. This affection occurred with the paronychia and was due to the same cause; namely, rowing a boat.

As regards the causes which operated to produce the disease, of ten cases where the causes were noted, in five the occupation was recorded as the cause. These five cases embraced four housemaids and one cabinet maker. In one case the cause was a slight cut; in another a slight burn; in another a slight bruise; and another was caused by rowing a boat.

Fourteen cases were recorded as having been opened: two, eight days after the beginning of the disease; five,

seven days after; six, five days after; and one, three days after.

All had suppurated, where this point was noted, except one case.

Ten cases were recorded as resulting in perfect cures; and one, as resulting in a permanent contraction of the finger. This last case was opened on the seventh day; but afterward the finger became very much inflamed and suppurated profusely.

This affection differs from paronychia only in the situation of the inflammation. It is of precisely the same character and demands the same treatment; namely, when the inflammation is not superficial, an early and free opening. It appears, however, to be rather less formidable than paronychia, and the results usually are much more favorable. In only one of eleven cases of inflammation of the first or second phalanges was the cure imperfect; and in this case the inflammation ran very high after the finger was opened, and resulted in permanent contraction of the flexors; while in nineteen out of fifty-five cases of paronychia proper, the cure was imperfect, and in some of these cases the last phalanx, or even more of the finger, was lost. Dr. Hamilton informs me, however, that in two or three cases, not recorded, he has seen an entire phalanx destroyed by necrosis.

PARONYCHIA MALIGNA

I have records of seven cases of paronychia maligna. Six of these cases were recorded by Dr. Hamilton, and one case I recorded at the clinical lectures by Prof. Gross, of the University of Louisville.

CASE I.—Joseph Carnin, aged nine years; admitted to the Buffalo Hospital of the Sisters of Charity, Oct. 19, 1848. Habit scrofulous; the extremity of the great toe of the left foot was swollen, red and slightly tender; the nail was black, rotten as pasteboard, and stood directly up from the matrix. This has been his condition for about a year.

A bread and water poultice was applied for the first twenty-four hours, and from this time ung. hyd. rub. or the ung. hyd. nit. was applied daily to the foot. The diet was generous and he was allowed occasional exercise. Under this treatment the malady gradually disappeared, the cure being accomplished in about three months.

CASE II.—Geo. Vangu, aged seven years. He had scarlatina six months ago and was very ill but now looks healthy. The par-

onychia began soon after his recovery from scarlatina. The nail is black and rotten; the affection is seated on the second finger of the right hand. Cause, constitutional and local. Treatment has been poultices, unguents, caustics, etc., etc. Corrosive sublimate wash increased the irritation; poultices gave most relief. Result is unknown.

CASE III.—Thomas O'Connor, aged six years. Five weeks ago he split the nail of his third finger; one week since, he bruised it. It has been treated with poultices. The nail became black and fell off but was reproduced, and of the same character as before, black and rotten. In this condition the finger remained many months, under different plans of treatment. Soothing poultices gave most relief, especially when combined with tonics and outdoor exercise. He was eventually cured.

CASE IV.—Henry W. Putnam, aged nine years. Disease affects the thumb. Cause, constitutional and local. As regards treatment, almost everything which has been recommended was tried. Six nails have fallen off successively since the disease began. The end of thumb is flat and the sides are puffed out and of a purplish red color; the lower half of nail is black and rotten; there is ulceration under the nail; the parts in the vicinity are red and puffy. The result in this case was a cure.

CASE V.—Williams, male, aged five years. Cause, probably constitutional. He was apparently in good health but had slight eruptions on various parts of his body. It has been treated with caustics, arsenic, corrosive sublimate, poultices, tonics, hyd. chlor. mite, etc., etc. The ulceration did not cease when the matrix of the nail was gone. Arg. nit. in substance, was first applied; but this only increased the irritation; hyd. chlo. corros. was then applied, with the same result. The end of the thumb was then shaved off but the ulceration attacked the stump, and it was finally necessary to amputate the last phalanx, when the wound slowly healed.

CASE VI.—Wm. Fitzgerald, aged eight years. He has paronychia maligna affecting the second finger of the right hand. Cause, constitutional and local. He ran a sliver of wood under the nail four months ago. It has been poulticed occasionally. The finger presents the usual appearance except that the nail is not blackened. He has a scrofulous ulceration and his mother is scrofulous. The poultices, with good diet and cleanliness, had the best effect. This case was cured after several months.

CASE VII.—Catharine Hynes, aged nine years, has paronychia maligna affecting the great toe of the left foot. Cause, constitutional and local. She has a scrofulous appearance and received a severe contusion upon the toe. The nail was removed by Prof. Gross, and the toe has the characteristic shovel shaped appearance. Treatment was the local application of blue wash, and slight mercurialization.

I saw the case some days after and it was progressing favorably.

This case I saw at the Louisville Marine Hospital, in 1854. It was treated by Prof. Gross.

Paronychia maligna, according to these observations, is a disease peculiar to children. Of the foregoing cases none were more than nine years of age. Three cases were nine years of age, and in one case the age was eight years. There was one case of seven years; one case of six years; and one case of five years of age. There were no cases of less than five years of age.

All the cases recorded by Dr. Hamilton were males; and the single case which was seen by myself was a female. This shows a very great predominance of males.

The affected hand or foot was not noted in a sufficient number of cases to make its consideration of value.

The great toe was affected in two cases; the thumb in two cases; the second finger in two cases; and the third finger in one case. Thus the hand was affected in five cases, and the foot in only two; showing that the disease was much more frequently seated in the finger or thumb than in the great toe, which I believe is contrary to the general opinion. When the foot was affected it was always in the great toe; but in the cases where the hand was affected it attacked the thumb or second and third finger. No cases were recorded of the disease seated in the first or fourth finger.

In all these cases but one the cause appeared to be either purely constitutional or at least partially so. In one case, however, the cause was apparently local (Case IV, H. W. Putnam), though the progress of the disease shows that the system was somewhat at fault. In three cases the cause was purely constitutional; and in three cases it was constitutional and local.

Such a variety of treatment has been practiced in these cases that its consideration, with reference to results, is of little value. Tonics, cleanliness and soothing applications appear to have had the best effect; and mild mercurial applications were used with advantage in two cases in connection with outdoor exercise, tonics and poultices. Caustics, where they have been used, have not been productive of any good effects but appear rather to have aggravated the disease.

Four cases (I. III. IV. and VI.) are known to have resulted in perfect cures. In three cases tonic measures and poultices were employed. In addition to these measures,

in one case, ung. hyd. rub. dilutum was used. In one case (V.) it was necessary to amputate the last phalanx of the thumb. In one case (II.) the result was unknown. I saw Case VII. several times at the Louisville Marine Hospital. It was progressing favorably and probably resulted in a perfect cure.

From these facts it may be inferred, that although the disease is likely to be protracted and tedious, yet with proper care a perfect cure is to be expected. Amputation of the affected part will rarely be necessary.

II

PHENOMENA OF THE CAPILLARY CIRCULATION—AN INAUGURAL DISSERTATION LAID BEFORE THE FACULTY OF THE JEFFERSON MEDICAL COLLEGE IN FEBRUARY, 1857

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THE statements which I shall make from my own observation concerning the capillary circulation are based upon examinations made from time to time during the past summer, eight of which have been carefully recorded. The recorded observations were made on the web of the frog, although I made examinations of the various other parts where the circulation can be conveniently exhibited, to which I shall refer.

The microscope used was the large instrument of Nachet; and unless otherwise stated, with a magnifying power of 165 diameters.

I shall first point out what I have found to be the most convenient methods of conducting examinations of the circulation in the frog, then proceed to describe the various phenomena of the circulation as viewed by means of the microscope, and then draw my deductions from these observations.

The parts of the frog which I have subjected to examination are the web of the foot, the tongue, the peritoneum and the lungs. All parts except the peritoneum should be examined by transmitted light; but in examining the circulation in the latter situation it is necessary to use reflected light.

It is exceedingly inconvenient to make observations while the frog has the power of motion, and in securing it to the frog-plate in a proper position, we are likely to interrupt or modify the circulation by constricting the vessels

with the bands which we must use. Under these circumstances medicated solutions can not conveniently be applied to the entire surface, and mechanical or chemical irritation of any part occasions struggles which greatly increase the difficulty of the experiment. By breaking up the medulla oblongata, or even the posterior part of the brain (for it is not easy to invariably reach the medulla without some practice), one is enabled to observe all the phenomena of the circulation with great facility, avoiding the necessity of forcibly retaining the frog in the desired position, with the consequent liability to constriction of the vessels and shifting of the field of observation. I shall hereafter refer to the experiments of E. Brown-Séquard, of Paris, and two of my recorded examinations, which show that observations of the circulation may be made with as much accuracy on a frog after the medulla has been destroyed as though it had not been subjected to the operation. The operation may be performed by introducing a dissecting needle into the cranium, a line or two behind the eyes, passing it backward and a little downward to the articulation of the spine with the skull, and then thoroughly breaking up the medulla. The web of the foot may be examined in the following manner: First break up the medulla oblongata in the manner just described; the frog will then remain perfectly motionless in any position. The web may be stretched over the opening in the frog-plate and secured in position by means of pins, care being taken not to extend the web too forcibly, and to put no pins above the foot, but nearly at the extremities of the toes, as in either case the circulation may be disturbed. The part should then be moistened, and the lenses of the microscope protected from the evaporation by a glass cover, broken to fit between the toes.

The entire surface of the frog should be moistened from time to time with cool water.

The magnifying power best adapted to such observations, is one of 150 to 200 diameters.

In examining the tongue, draw it out of the mouth and stretch it so as to form a thin transparent film by means of the forceps and pins. The circulation may be exhibited in the peritoneum by merely exposing that membrane and examining it with a power of 60 or 70 diameters by reflect-

ed light. The method of exhibiting the circulation in the lungs of the frog is much more complicated and difficult than either of the preceding experiments, but when successfully performed, it is one of the most beautiful and curious demonstrations in the whole range of microscopic work.

Dr. Robert Willis, in his edition of "Wagner's Physiology," refers to the appearances of the pulmonary circulation in the water newt. He directs that the newt be strangled after an inspiration. "The abdomen is then to be laid open, and the entire animal, being held in the hands, is placed upon a glass plate as a 'porte-objet,' and one of the lungs brought into the field of view." He observes, however, that the circulation lasts but a short time. The frog appears to me to be a much better subject for this experiment; and as I have never seen the process of showing the pulmonary circulation in this animal detailed in the books, I shall describe it with some minuteness as practised by Prof. John C. Dalton, of New York, and as repeated frequently by myself.

In undertaking it, a large sized frog should be selected. After having broken up the medulla oblongata, a ligature is to be placed around the larynx in the following manner: The mouth being widely opened, the larynx is seen just in front of the oesophagus. A ligature is now carried just under the mucous membrane by means of a small curved needle. This is effected by making four or five stitches, the needle being introduced at the point where it came out at each preceding stitch, so that the ligature shall smoothly encircle the larynx and its extremities emerge at the same point. This being done, a small blowpipe is introduced into the windpipe and the ligature is held in readiness to be drawn tight by an assistant when required. The lungs must now be moderately distended and the ligature tightened, at the same time removing the blowpipe. If the side is now carefully opened the lung will protrude and may be examined by transmitted light.

It is very much more difficult to exhibit the circulation in the lungs than in any other part. The chief difficulties to be encountered are the following: First, it is no easy matter to fix the ligature properly around the larynx; but when this has been done, if the lungs are distended too

forcibly, they will either burst or the circulation will be greatly impeded; and if not distended sufficiently, they will not protrude when the side is opened. There is, also, always some difficulty in introducing the blowpipe, and its delicate orifice is often occluded by the secretion of the part. When successful, however, in exhibiting the circulation in the lungs, the capillaries are seen encircling the air-cells, which are quite large in the frog. This is an extremely beautiful and interesting sight—but more as a scientific curiosity than as a field for useful investigation. It was observed by Dr. Willis, and confirmed by Wagner and Gluge, that the transparent plasma which is found occupying the space next to the walls of the capillaries in most situations, while the blood-disks occupy the centre, constituting the still layer of Kirkes, is not observed in the capillaries of the lungs; in other words, the vessels are crowded to their very walls with corpuscles.

For this remarkable deviation from a general law they offer no explanation.

I have never observed this peculiarity, as my attention was not directed to it when examining the pulmonary circulation. Those who believe that the heart is solely instrumental in propelling blood through the capillaries would not be able to account for this phenomenon; but it seems to me it can be explained in the following manner: The blood circulating in the systemic capillaries nourishes the tissues by the liquor sanguinis, and thus the attractive vital force operates on this constituent. The plasma then is nearest the tissues and next the walls of the vessels; but the pulmonary capillaries are for the aëration of the blood, a process which is effected by the globules and not by the plasma, since the great mass of blood is not sent to the lungs for purposes of nutrition, but for aëration; hence, the globules, which here feel the force of attraction for oxygen, occupy the space next the walls of the vessels.

Taking the view which I do of the causes of the capillary circulation, this explanation is satisfactory.

Before proceeding to describe minutely the phenomena of the capillary circulation, I shall briefly consider the anatomical structure of the capillaries and of the blood.

Ch. Robin recognizes three varieties of capillaries. The first variety is $\frac{1}{800}$ to $\frac{1}{350}$ of an inch in diameter, and

is composed of a transparent homogeneous membrane, $\frac{1}{300}$ of an inch in thickness, with nuclei, and sometimes nucleoli, projecting into the calibre of the vessel. The nuclei are oval, with their long diameter in the direction of the vessel. These are embraced under the head of the "true capillaries" of Prof. Kölliker.

The second variety, M. Robin describes as having two coats: the membrane with the longitudinal nuclei of the first variety, and investing it, a second membrane with transverse nuclei. The diameter of the second variety varies between $\frac{1}{100}$ and $\frac{1}{150}$ of an inch. This variety also probably comes under the head of the "true capillaries" as described by Kölliker, though he does not mention the second investing membrane.

The third variety, M. Robin calls venules and arterioles; Kölliker, venous and arterial transitionary vessels. Their diameter is $\frac{1}{10}$ to $\frac{1}{15}$ of an inch, and they have added to the two coats of the second variety a third coat of areolar tissue. It seems to me most convenient and proper to consider the first two varieties of M. Robin, or the "true capillaries" of Prof. Kölliker, simply as capillaries (their tunic being a prolongation of the inner coat of the arteries), and the third variety of M. Robin as venules and arterioles. One may easily distinguish the arterioles from the venules, by noticing that the arterioles give off branches, while the venules receive them; that the arterioles diminish in size in the direction of the current of blood, while the venules increase in size.

The blood consists of a transparent plasma holding two kinds of corpuscles in suspension, called the red and white, or colorless. In the human subject the red corpuscles are disks like pieces of coin, but thinner in the centre than at the edges. They have no nuclei, though the difference in thickness causes the centre to appear dark when the edges are in focus. They are $\frac{1}{300}$ of an inch in diameter. The white corpuscles are larger than the red, being $\frac{1}{200}$ of an inch in diameter; they are globular, white and granular. If water is applied to them they are rendered transparent, and we can distinguish a nucleus. They are much less abundant than the red corpuscles. In the frog, the red corpuscles are oval and large, with a central rounded nucleus. They are $\frac{1}{100}$ of an inch in their long diameter.

The white globules are smaller and proportionally more abundant than in man. The blood-disks in nearly all animals are red by reflected light, but of a pale amber color by transmitted light.

In a paper communicated to the "Medical Examiner," August, 1852, by E. Brown-Séquard, M. D., of Paris, entitled "Experimental Researches applied to Physiology and Pathology," I find some very interesting observations on the effect, or more properly the absence of effect on the capillary circulation, of the section of various nerves. This observer, with the assistance of Dr. Siebert, found, "after the section of all the nerves (the sympathetic and cerebro-spinal) in the legs of a number of frogs, that there was no appearance of trouble in the capillary circulation, either in one hour or three or four days after the division of the nerves." He concludes from another experiment that the nervous action (that of the sympathetic as well as the cerebro-spinal nerves) is not necessary for the change of color of the blood in the capillaries. It is proved by this experiment that the capillary circulation is not immediately dependent in any measure on nervous influence.

A curious fact has been observed by Bernard; viz., that after a section of the sympathetic in the neck, the corresponding side of the face, and more particularly the ear, becomes warmer and more sensitive than the other side. The bloodvessels appear more abundant than before and are enlarged. Brown-Séquard has repeated this experiment and concludes that the increase in temperature and sensibility is due merely to passive dilatation of the vessels from paralysis of their coats and consequent congestion. I have myself seen the experiment performed by Prof. Dalton, of New York, and concur with him in the opinion that the increase in temperature and sensibility is due rather to an exaggeration of the nutrition of the parts; for specimens of blood drawn from the two ears have been compared, and there has been found a marked difference in their actual chemical composition.

These considerations are interesting in connection with animal heat as produced by the molecular changes in the various tissues, and appear, also, to bear in some measure on the subject of the capillary circulation.

I shall hereafter take the ground that the capillary cir-

ulation is in a great measure dependent upon an attraction of a chemico-vital character between the tissues and the nutrient fluid.

Now, if the nutrition of the part is augmented, the congestion is due to the greater attraction of the tissues for the blood, the capillaries being first affected by its influence. The nutrition is affected, because the blood actually undergoes greater changes than on the other side. The capillary circulation, then, in this case seems clearly to be in a measure dependent on the process of molecular regeneration and disintegration. There is no new action induced in the part, but simply an augmentation of the usual processes; and if this is so, a cause of the capillary circulation is a chemico-vital attraction of the tissues for the blood. The fact that there can be a greater supply of blood, circulating with greater force, on one side of the body than in the corresponding part on the other side, seems to me an insuperable objection to the idea that the heart alone circulates the blood in the capillaries; but I have anticipated, in some degree, the points which I shall hereafter consider more fully.

When I began to describe the manner of making observations on the capillary circulation in various parts, I assumed that destruction of the medulla oblongata had no appreciable effect on the capillaries. Brown-Séquard has demonstrated by experiment, that frogs are able to live perfectly well for three or four months after extirpation of the medulla, and that all the functions, except pulmonary respiration, go on apparently as usual.

Before I met with these observations, I made two experiments with reference to the reliability of observations made on a frog after breaking up the medulla or the posterior part of the brain.

In my first experiment the posterior part of the brain was broken up in an unsuccessful attempt to reach the medulla.

OBSERVATION I.—The circulation was observed for seven hours and was but slightly retarded when the experiment was concluded. For the first two hours the circulation appeared as usual. I have made many unrecorded observations on this point and have always arrived at the same result; I have introduced a dissecting needle at the back of the head, sometimes reaching the medulla and some-

times not, but always rendering the frog perfectly quiet and manageable; and I have been unable to discover any effects upon the circulation or the phenomena produced by irritants.

After making this experiment I made several dissections so as to be able to reach the medulla oblongata with certainty, and succeeded in destroying the medulla in the following observations:

OBSERVATION II.—I examined the circulation for five hours with the same results as in the preceding experiment. There was no alteration from the appearances of the circulation in the uninjured frog, at least for the first two or three hours.

From these observations added to my unrecorded experiments I have no hesitation in saying that observations on frogs after breaking up the medulla oblongata or the posterior part of the brain are quite as valuable as those made on uninjured frogs; therefore all the subsequent observations were made after breaking up the medulla, unless otherwise stated.

Dr. Wilson Philip made an experiment which is interesting, though not throwing any light upon the causes of the capillary circulation. "While Dr. Hastings was observing the circulation, he crushed the brain by the blow of a hammer. The vessels of the web instantly lost their power, the circulation ceasing; an effect which we have seen cannot arise from the ceasing of the action of the heart. (Dr. Philip here refers to experiments by which it is ascertained that the blood will circulate for several minutes after the interruption of the heart-action.) In a short time the blood began to move, but with less force." I may here add the notes of a similar experiment performed by myself:

OBSERVATION III.—The brain of the frog was crushed while Prof. Flint was examining the circulation, which was brisk and regular; the motion instantly ceased, but began again in a few seconds, though it proceeded more slowly. This observation in every respect confirms that of Dr. Philip.

This, as I have before remarked, cannot be thought to show that the capillary circulation is dependent upon nervous influence, but merely that a violent shock is able to arrest momentarily all the vital functions. In several of my observations, I have minutely recorded the appearances of

the capillary circulation and have noticed the following phenomena:

OBSERVATION IV.—I examined the web of a young frog.

From a careful and prolonged examination, it is evident that there is a difference between the modes of circulation in the arterioles and the venules. The blood moves more freely in the former and the motion appears to be dependent on an attractive force. This is not so evident, however, here as in the capillaries; there the blood shoots off to different parts of the tissues in a manner which cannot be dependent upon a "*vis a tergo*." It also moves much more rapidly in some of the capillaries than in others, the velocity varying in the same vessel at different times. In the venules, the movement is more sluggish, the globules apparently crowding each other along, and on careful examination making a decided contrast to the movement in the arterioles. The number of colorless globules is greater in the venules; they adhere to the walls of the vessels and appear to be pushed along by the central mass, moving very much more slowly and occasionally remaining stationary for a time.

OBSERVATION V.—In this observation, the same points attracted attention as in the preceding one, and in addition, the following phenomena were noted:

A small transverse capillary, admitting but a single globule at a time, was abruptly bent at a certain point. The globules passed along in single file, irregularly isolated from each other, and were bent nearly double in passing the sudden turn in the vessel. This caused the globules to present a singular appearance at this point; they seemed to move by volition, like animate beings. The motion of the globules under the above circumstances seemed to indicate an attractive force.

In several instances the walls of the vessels were distinctly seen; they were perfectly motionless, evidently taking no active part in the circulation. The darting of single globules through small vessels, at a velocity greater than the velocity of the circulation in the vessel from which they branched, was repeatedly noted.

OBSERVATION VI.—The points noticed in Observation IV were here confirmed. I was forcibly struck with the great difference in the velocity of the circulation in different parts of the field, both in vessels of the same size and of unequal sizes. I also remarked a difference of velocity in the same vessels, especially capillaries, at different times.

An attractive force is evident; and a certain condition of the disks is necessary in order that the force should operate. This condition, it may be presumed, is brought about by respiration.

The appearances of the capillary circulation in the web of the foot may be described as follows:

When the web is subjected to examination in the man-

ner already described, there are vessels of various sizes in the field, consisting of arterioles and venules, which vary most in their diameters, and the true capillaries which are all of nearly equal diameters. The blood is seen coursing along these vessels with great rapidity, especially in the arterioles, where we may observe a slight pulsatory movement.

In the arterioles, blood moves with unvarying rapidity as a general rule; and here especially we notice a space next the walls of the vessels, which is not occupied by the red globules, but along which the colorless globules move at a diminished rate, appearing to have a tendency to adhere to the walls of the vessels, and sometimes even remaining entirely stationary for a time, to be pushed along again by the central mass. This constitutes the "still layer" of Kirkes.

The white or colorless corpuscles are much fewer than the red and they move at least ten or twelve times more slowly than the central mass. On careful examination I have been able to note a decided difference between the circulation in the arterioles and the venules. In the latter the movement is not so rapid, the globules appearing to be impelled more by a "*vis a tergo*" and to feel less the "*vis a fronte*," which seems to operate in the arterioles. The comparative number of the white corpuscles is greater, but the "still layer" appears to occupy a smaller proportion of the calibre of the vessel.

In the true capillaries the movements are less regular and apparently are dependent in a great measure on a force which acts directly upon them; the "capillary power," as it is designated by Dr. Carpenter. This will be more fully touched upon presently in considering the causes of the capillary circulation.

In the true capillaries the blood moves in every possible direction, at different rates of speed in different vessels and at different times in the same vessel. In one instance I remarked a capillary branching from a vessel at an obtuse angle (that is, turning almost directly opposite to the current in the main vessel), and individual globules shooting through it with great rapidity. In many instances, I observed a complete stasis in one or two of the capillary vessels, but it existed only for a moment and the current began

again with its original vigor. Dr. Carpenter has remarked a stasis followed by a current in an opposite direction.

It frequently happens that a globule is caught at the point of junction of two vessels and remains stationary until it is carried along by the current of blood. Globules are frequently bent upon themselves as they pass from one vessel to another, but so soon as the cause is removed they regain their original conformation.

The walls of the vessel are motionless, and they do not take an active part in the normal circulation as was supposed by some of the older writers.

Pigment-cells are observed scattered over the field, when they are very abundant obscuring the view of the circulation; therefore it is best to select a light colored frog for demonstrations.

The pavement variety of epithelium may also be seen.

This is a description of the capillary circulation as it appeared to me under the most favorable circumstances: more minute, but not otherwise differing from the ordinary description in works on physiology.

I now come naturally to a consideration of the causes of the capillary circulation. I say causes, because I shall take the ground that it is not produced by a single cause; namely, the heart's contraction, as was supposed by the great discoverer of the circulation. While it may be that the action of the heart is sufficient to propel the blood through the whole round of the circulation, as is contended by Magendie, by Dr. Allen Thompson, in the "Cyclopedia of Anatomy and Physiology," Dr. Kirkes and others, I believe that there are other causes which operate and are able to carry on the circulation unassisted, as was the case in the acardiac fœtus of Dr. Houston, reported in the "Dublin Medical Journal," 1837, where, of course, the circulation was stopped at the birth of the child by the want of due aëration of the blood.

Harvey, followed by Magendie, Kirkes and other eminent physiologists, supposed that the heart was alone concerned in the production of the circulation, and some very striking arguments were made use of to prove it. It is found that under the most favorable circumstances a very inconsiderable force is required to propel a bland fluid from the arteries through the capillaries and out again by the

veins. The pulsative movements, which are observed under some circumstances in the capillaries, is also brought forward as an argument. Dr. Kirkes dismisses the subject with the remark that "there is no need of an hypothesis of any action of the capillaries for regular propulsion of the blood through them, nor is it probable they have such an office." This appears to me a most unphilosophical mode of treating a very important subject. The circulation of the blood is a process immediately necessary to existence; and even admitting that the action of the heart is quite capable of carrying on the circulation, it would not be out of place to inquire if there be not some other force which also operates to this end, and can take on, in some degree, the function of circulating the blood, should the heart become weakened from any cause. In the performance of that essentially vital function, respiration, we commonly use but about one-third of the entire capacity of the lungs; and though the lungs seem to be only aërating organs, they divide that function with the skin. One might as well say that as the diaphragm is sufficient to carry on respiration, there is no need of supposing that there are any other respiratory muscles.

There are several phenomena which are difficult of explanation on the theory of the sole action of the heart in producing the circulation. In the first place it is difficult to understand how the heart could impel the blood through the second set of the capillaries in the portal system. Then the experiments of Dr. Dowler show that the blood probably circulates in the capillaries in patients dead from yellow fever, after the heart's action has ceased.

In the frog, Dr. Carpenter asserts, and I have myself seen that the blood will circulate in the capillaries after complete excision of the heart. Carpenter also mentions instances where the heart has suffered such a degree of fatty degeneration or displacement that there existed scarcely a trace of muscular fibre, and the circulation must have been chiefly dependent on the "capillary power." Hassall records a most remarkable phenomenon; namely, the continuance of circulation in a portion of the tongue which had been entirely detached from the body. He states that while examining the tongue of a frog, a small portion was torn off, which he placed between two plates

of glass and was astonished to see the circulation continuing in many of the smaller vessels with unabated vigor. This phenomenon he observed for several hours, in connection with several medical gentlemen; and on examining it the next day, preserving it under water in the interval, the circulation still continued to some extent. This seems almost incredible; but coming from such authority the fact can not be doubted. Hassall appears to have made no subsequent experiments with reference to this point. After seeing this statement, I made two or three experiments, and once saw a slight movement in a portion of the tongue entirely detached; these experiments were not made, however, under favorable circumstances, the weather being cold, and the frog in a state of torpor until partially aroused by immersion in tepid water.

A case is mentioned by Dr. Carpenter of an acardiac foetus which was subjected to examination by Dr. Houston, where the organs were tolerably well developed, with the exception of the heart, and the circulation could be effected only by the "capillary power." The cases which I have described are amply sufficient to disprove the theory that the heart is the sole cause of the circulation. In addition, the phenomena of inflammation as seen under the microscope; the normal appearances of the capillary circulation, which appear to the eye to be in some measure dependent on an attraction of the molecules of the tissues for the blood; the experiment of the section of the sympathetic in the neck of the rabbit, which I have previously noticed, and which produced an augmentation of this attractive force in the corresponding ear and side of the face; and comparison with the circulation in some aquatic plants, which is not dependent upon the action of a heart; all these go to show that the heart alone does not carry on the circulation.

Prof. Draper, of the University of New York, has proposed a theory in regard to the circulation, which makes the heart of minor importance. His is the theory of capillary attraction and affinity. He starts with the proposition that, "if two liquids communicate with each other through a capillary tube, for the substance of which they have affinities of different intensities, movement will ensue; the liquid having the highest affinity will occupy the tube, and may

even drive the other from it; the same effect will ensue in a porous object." He believes that this is the main cause of the circulation; namely, an affinity between the blood and the tissues; that thus the blood is forced into the veins; and that the action of the heart is limited to filling the arteries and presenting a supply of blood to the capillaries. The blood circulates in the lungs chiefly on account of its affinity for oxygen.

This theory can not be sustained. The heart undoubtedly has a much more important office in the production of circulation. When a small artery is cut the blood is seen forcing itself in a jet to a distance of several feet; and this happens after it had entirely lost the influence of the capillary force. The illustration of Prof. Dunglison; namely, the law that fluids confined in tubes will rise to the same level, and that thus the blood in the veins, by a simple hydrostatic principle, would rise as high as the right auricle in a line with the blood in the left ventricle, shows how slight a force from the heart would be propagated through the capillaries to the veins and be sufficient to return the blood.

Dr. Dowler, of New Orleans, believes in a distinct capillary action. In some of the experiments which he adduces in support of his position, and which are noticed by Prof. Dunglison in his "Human Physiology," bodies of yellow fever patients were carried to the dissecting room a few moments after death. "The external veins sometimes became distended, and when punctured, the blood flowed in a good stream; the operation of bleeding at the arm was imitated, and as the muscles were moved, the blood shot forth for some distance." Other experiments on the veins, of a similar character, are recorded by him.

These observations seem to show that there is some action in the capillaries after death, and inferentially during life, which is independent of the heart's action. The entire emptying of the arteries after death cannot be satisfactorily explained by mere contraction of the vessels.

What causes seem to operate to produce the capillary circulation, judging merely from the appearances under the microscope? In the observations which I have recorded on this point, I noted an irregularity of the movement in the capillaries, both in different vessels at the same time and in the same vessel at different times; the irregularity

sometimes amounting to entire cessation of the circulation in a single vessel, and then a current in an opposite direction; a shooting off of single globules through vessels which were before empty; the darting off of globules through capillary branches with a velocity greater than that of the blood in the main vessel; and in short, all the phenomena which are presented to the eye seem to indicate that there is an attractive force, resident in the solid particles, which operates on the blood in the capillaries.

I am not supposing the existence of a force with the operation of which physiologists are unacquainted. The present school of physiology teaches that the processes of nutrition, of molecular disintegration and of secretion are dependent on a vital force resident in the solid particles of the organism which are essentially vitalized. Inflammation is now supposed to be due to a perversion of this force.

What other explanation is there of the fact that every tissue takes from the mass of arterial blood the substances which are required for its nutrition? The blood sent to the systemic capillaries by the heart is the same in all parts of the body; but when the great change which is effected in the capillaries has taken place, the blood which has thus been rendered venous is not the same in all the veins; for example, the blood in the renal vein is almost as florid as arterial blood.

The existence of a distinct capillary action is now believed by the highest authorities. Lehmann believes that a chemico-vital attraction of the blood for the tissues, together with the physical capillary attraction, produces the movement of the blood in the capillaries and forces it into the veins. Dr. Carpenter believes that there exists a "capillary power" which is superadded to the force of the heart. Prof. Dunglison teaches that there is an independent power resident in the tissues about the capillaries, and that, "by the united action of the heart, arteries and capillaries, or intermediate system of vessels, the blood attains the veins." Even those who recognize the heart as the only efficient organ of circulation admit that the capillaries possess a "distributive force;" that is, though the circulation is effected by the heart's unassisted action, the tissues have an attraction or affinity for the blood, which distributes it for their nutrition to each and every part of the body.

Taking into consideration everything that I have seen bearing on this point, it seems to me to be clearly proved that the normal capillary circulation is dependent, in the first place, on the action of the heart. It cannot be denied that the heart has a considerable share in producing capillary circulation. Taking into account the conditions of the blood and vessels, apparently a slight force is capable of propelling the blood through the capillary system. When a small artery is divided, the force with which the blood flows out is considerable and appears sufficient to exert a decided effect on the motion of the blood in the capillaries. It is impossible to estimate with much accuracy the proportional influence which the heart has in producing the capillary circulation. The vital affinity between the tissues and the blood, which I suppose to be the other power concerned in this function, never ceases; still, as the action of the heart is frequently much interfered with, as in cases of excessive fatty degeneration, and as the heart has been removed from the frog, the capillary circulation nevertheless continuing, I cannot think that its power is greater than the active force, or Carpenter's "capillary power," which I hold to be essentially concerned in the performance of this function. The value of the heart's action is also variable, both in different individuals and in the same individual at different times.

The only other force which has any share in the production of the capillary circulation, except, perhaps, a slight suction force from the veins, is the "capillary power." This seems to me to play the more constant and effective part. When this ceases to act the animal dies and the blood refuses to circulate in spite of the heart. This is the great vital force of nutrition which is constantly operating and which is so wonderful and inexplicable. It is a fact that there is such a force and that it continually acts; but what it consists of or what is its essential character is beyond the wisdom of man to explain. It is life. Finally, the following inquiry suggests itself: What conditions are necessary to the healthy performance of the capillary circulation?

First, a healthy condition of the vital particles, which is produced by healthy nutrition. Second, a certain condition of the blood, which is produced by respiration.

No arguments appear to be necessary to prove the

former statement; but I have made experiments, which I shall proceed to describe, which conclusively establish the second point.

The following experiment, made by Dr. J. Reid, and reported in the "Edinburgh Medical and Surgical Journal," April, 1841, is quoted by Dr. Carpenter:

Dr. Reid found that when the ingress of air through the trachea of a dog was prevented and asphyxia was proceeding to the stage of insensibility, the pressure in the femoral artery, indicated by the hemadynamometer, was much greater than usual.

Upon applying a similar test to a vein, however, the pressure was proportionally diminished; whence it became apparent that there was an unusual obstruction to the passage of the venous blood (the blood being venous in the arteries) in the systemic capillaries.

Before seeing an account of this experiment, I had made the following observations, carefully recording them, with reference to the same point:

OBSERVATION VII.—The medulla of a medium-sized frog was broken up and the web submitted to microscopic examination. The frog was bathed with sulphuric ether, care being taken not to allow the ether to touch the web under examination, and the circulation was watched for ten minutes. No effect could be discovered. The object of this experiment was to determine whether the phenomena in the succeeding experiment were in any degree dependent on the ether which is contained in collodion.

The frog was then painted over with an impermeable coating of collodion, care being taken as before not to touch the web. The effect on the circulation was immediate. It instantly became less rapid, until at the expiration of twenty minutes it had entirely ceased.

The smaller vessels were the first to become affected, the larger arterioles resisting it longest. One of the first effects was a pulsatile movement in vessels where the blood had previously flowed in a continuous stream, showing, as it seemed, that the attractive force was lost, but that the heart's action was felt.

The fact of the first arrest of the blood in the capillaries seemed to indicate that the blood was unfit to supply the wants of the tissues, and that the attractive force had ceased to be operative. The arrest of the circulation was steady, and at the expiration of twenty minutes the motion had entirely ceased.

The entire coating of collodion was then instantly peeled off, and the effect on the circulation was instantaneous. Quite a rapid circulation immediately began, but it soon began to decline, and in twenty minutes had almost ceased. The heart was now exposed

and found contracting regularly. In this experiment all respiration was abolished, the medulla being broken up and an impervious coating applied to the entire surface.

OBSERVATION VIII.—I painted a frog with a thick coating of collodion without destroying the medulla. It struggled vigorously at first, but soon became quiet and the web was put under the microscope.

The circulation was affected in the same manner as in the preceding experiment and entirely ceased in twenty-five minutes.

During the first few minutes the nostrils dilated and contracted rapidly but soon became motionless. Care was taken not to obstruct the nostrils with collodion, although it was applied effectually to all other parts except the foot under observation.

The experiment of Dr. Reid proves this fact inferentially; namely, that the blood, deprived of oxygen, as in asphyxia, is retarded in the systemic capillaries; but the experiments just related bring the processes directly under the eye; and one can see clearly that when the blood is not aerated it will not circulate, although the heart contracts; and that it is retarded in the capillaries. My second experiment demonstrated the comparatively small part which the lungs of the frog take in respiration; the blood circulating in the frog, in which the pulmonary respiration was not interfered with, only five minutes longer than in the frog after destroying the medulla. Capillary circulation will go on in the lungs of the frog after tying the trachea, as I stated when describing the circulation as seen in various parts of the animal, the blood being sufficiently aerated by means of the skin.

Thus it is experimentally proved that an oxygenated state of the blood is an indispensable condition for its circulation through the capillaries. When the process of respiration, or aëration of the blood, is interrupted, the blood cannot circulate. This is an acknowledged fact; but I have shown, by the preceding experiments, that in asphyxia the impediment to the circulation is in the capillaries; that the condition of oxygenation is necessary to the performance of the vital functions; and it may be that the entire want of the "capillary power" throws all the onus on the heart, and that the heart is insufficient for the labor. In one of my experiments, after the capillary circulation had entirely ceased, the chest was opened and the heart was found beating regularly.

III

EXPERIMENTS ON THE RECURRENT SENSIBILITY OF THE ANTERIOR ROOTS OF THE SPINAL NERVES

Published in the "New Orleans Medical Times," in 1861.

THERE are few facts in physiology better known and more generally admitted than those which have reference to the properties of the two roots of the spinal nerves. The anterior roots are motor and the posterior roots are sensory. Like most important discoveries, however, the credit of its authorship has been somewhat disputed, though it is now usually conceded to Sir Charles Bell. It is a curious fact, nevertheless, that in 1809, two years before the appearance of Sir Charles Bell's first essay, Mr. Alexander Walker, an English physician, advanced the idea that the two roots of origin of the spinal nerves had different properties; but he supposed that the posterior roots were motor and the anterior roots sensory. To support this view, which was a mere supposition, Walker brought neither physiological nor pathological proofs; but in 1811, Charles Bell made the great discovery with which his name is connected; viz., that the posterior roots conducted sensations and that their irritation produced no movements, while the anterior roots were motor, as proved by the occurrence of muscular movements when they were stimulated. Bell, however, was not a vivisector; his experiments were chiefly on rabbits, which he killed suddenly, opened the spinal canal and irritated the posterior and anterior roots of the nerves, the experiments resulting, as just stated, in movements of muscles when the anterior roots were stimulated, and none when the same stimulation was applied to the posterior roots. These experiments were repeated by French and German physiologists, among

whom were Müller, Valentin, Magendie and Longet. Longet, especially, carried Bell's experiments on the nerve-roots to the columns of the cord and demonstrated that the anterior columns were motor while the posterior were sensory. He also made a number of confirmatory experiments upon the roots of the nerves in living animals.

The experiments which are chiefly to be noticed in the present communication were made by Magendie; who, though many physiological facts had of course already been arrived at by experiment, may be said to be the father of the experimental school of physiology. He made experiments, which were published in 1822, upon the roots of the spinal nerves, and found that while the posterior roots were purely sensory, the anterior roots were not, in all of his observations, purely motor, but sometimes possessed a slight degree of sensibility. These experiments he repeated in 1839 and was able to establish at that time a certain degree of sensibility in the anterior roots. He also showed that the facial possessed some sensibility and that this was derived from the fifth pair. This he called the "recurrent sensibility;" and these experiments tended to show that the views of Sir Charles Bell and his followers had been too exclusive; that the anterior, or motor roots possessed a certain degree of sensibility, though not so acute as in the posterior roots. Here is met a curious event in the history of the recurrent sensibility: Magendie's experiments, being in a manner opposed to the views of Bell, which were then universally received, attracted considerable notice; but when, after 1839, he attempted to repeat them, he utterly failed, and finally abandoned the ground that he had taken—one of the many examples of the honesty of description which mark the experiments of this distinguished physiologist. It was not until 1846 that Bernard revived "recurrent sensibility" and succeeded in again demonstrating it. He remembered that in 1839 the experiments for the lectures of Magendie were prepared in the morning, and that the animals used for the purpose of demonstrating recurrent sensibility were thus permitted a period of repose before demonstrations were made during the lecture, which took place in the afternoon. He himself had made operations on the spinal cord and roots of the

nerves, and had found that after the operation of opening the spinal canal, which is exceedingly painful and tedious, the general sensibility of the animal was blunted. The state of the nerves, then, was more natural after the animal had been permitted to recover from the first effects of the operation than immediately after the exposure of the roots. Carrying this idea into practice, he opened the spinal canal in dogs and allowed them two or three hours' repose before he made his observations on the roots of the nerves. In experiments conducted in this way, especially in dogs that were vigorous and well nourished, he always found the anterior roots of the nerves sensitive. He found, also, that the sensibility was derived from the posterior roots; for the division of these immediately abolished the sensibility of the anterior roots. He made in addition some interesting observations upon the disappearance of sensibility from exhaustion, anesthetics and other causes. He showed that sensibility first disappeared in the anterior roots, then in the periphery and last in the posterior roots. When the sensibility reappeared, it was first manifest in the posterior roots, then in the periphery and last in the anterior roots. These experiments of Bernard have fully established the fact of recurrent sensibility; but so far as I am aware, they have been repeated and confirmed only by Schiff.

As I have lately had occasion to repeat these experiments at the New Orleans School of Medicine and to demonstrate to the class, in my regular course of lectures, recurrent sensibility, I have thought the subject sufficiently interesting to put upon record my own experiments which confirm the view held by Magendie, in 1839, afterward abandoned by him but confirmed in 1846 by Bernard.

Bernard's experiments were made before the use of ether as an anesthetic; but Schiff, who repeated these experiments at a later date, always made use of ether in the operation of opening the spinal canal. This of course abolishes pain during the preliminary operation; and in the course of one or two hours the animal entirely recovers from its effects and is ready for the observations on the nerve-roots. It is best to select a vigorous healthy dog for the operation as the sensibility is then much more marked. The most convenient situation, also, at which to

open the spinal canal is in the lumbar region at the point of junction of the iliac bones with the spinal column.

EXPERIMENT I.—February 15, 1861, 11 A. M. A vigorous medium-sized dog was completely etherized, placed on his belly on the table, with a billet of wood under the lumbar region to make this part of the spinal column prominent. The hair was then cut from the parts to be incised, and a longitudinal incision about four inches in length was made just to the left of the spinous processes of the lower lumbar vertebræ. This incision was then carried down by the sides of the spinous processes to their junction with the laminæ. The laminæ of the fifth, sixth and seventh lumbar vertebræ were then denuded of their muscles and were cut through vertically by a fine saw carried as near the spinous processes as possible. The laminæ were then divided near the transverse processes, by a cut of the saw parallel to the first but directed obliquely inward. There is danger in making this second cut of wounding the nerves as they emerge from the spinal canal and also of opening the vertebral sinus; but this may be avoided by cutting with great care, not going through the laminæ entirely but breaking them off by prying with a chisel introduced into the cut next the spinous processes. In opening the spinal canal the roots of the fifth pair of lumbar nerves were divided. The roots of the sixth pair, however, were intact. These roots were separated carefully by a delicate blunt hook, threads were passed beneath them, the wound was closed by sutures and the animal set at liberty. After recovering from the effects of the ether, it was discovered that his left posterior extremity was partially, though not completely paralyzed, owing to the injury to the nerves during the operation of opening the spinal canal.

February 16, 11 A. M. Twenty-four hours after the operation the wound was opened; the discharges, which had been considerable, were removed, and irritation by means of pinching with forceps was applied to the roots of the nerves. Both roots were sensitive, as manifested by the cries of the animal, but the sensibility of the posterior root was by far the more acute.

The wound was then again closed and the same experiments were made before the medical class, at 2 P. M. The sensibility of the posterior root was then acute; but the sensibility of the anterior root had considerably diminished, probably on account of exhaustion produced by the experiment at 11 A. M.

EXPERIMENT II.—February 16, 11.30 A. M. The dog used in this experiment was a larger, younger and more vigorous dog than the one used in Experiment I. The animal was etherized and the incisions made, denuding the spinous processes and laminæ of the sixth and seventh lumbar vertebræ, as in Experiment I, with the difference that the operation was made on the right side. The laminæ of the sixth and seventh lumbar vertebræ were then removed without wounding the roots of any of the nerves. This was done by making the cut with the saw farthest from the spinous processes extend only partially through the bone and then removing

the laminæ by prying them off with a chisel. The roots of the sixth lumbar nerves were then isolated, and threads of fine silk were passed beneath them. The wound was then closed and the animal set at liberty. The operation lasted about three quarters of an hour.

2 P. M. The animal was exhibited to the medical class and the following observations were made. The slightest touch of the posterior root produced intense pain manifested by cries. Upon pinching the anterior root, the animal cried, evidently suffering pain though not so intensely as when the posterior root was barely touched. Care was taken in irritating the anterior root not to touch the posterior root. The posterior root was then divided, its section causing intense pain, and the anterior root was again irritated. Now, however, its sensibility had entirely disappeared, and it could be contused in the roughest manner without producing any evidence of suffering.

The operation for the purpose of exposing the spinal cord is quite difficult and tedious, on account of hemorrhage, which is sometimes abundant, and difficulty in avoiding injury of the roots of the nerves and opening the vertebral sinus. These accidents can be avoided, however, with a little practice. The instruments necessary for opening the spinal canal are a small saw, a Hey's saw, a pair of small bone-nippers and a chisel. When the laminæ of the vertebræ have been removed, the spinal cord is exposed, surrounded by a certain quantity of fat which should be carefully removed with forceps. A pair of small blunt hooks are then necessary for the purpose of isolating and catching up the roots of the nerves. It is best then to pass a fine thread under the nerves before closing the wound, so as to be able easily to find them again. The wound is then to be closed and the animal allowed to repose for two or three hours, when it will have recovered entirely from the effects of the operation and the roots of the nerves will have regained their normal sensibility.

I have thus detailed two experiments which show in a marked manner, especially Experiment II, that the anterior roots of the spinal nerves are not exclusively motor but that they possess a certain degree of sensibility; that this sensibility is recurrent and is derived from the posterior, or sensory roots; and that after the division of these roots, it is immediately lost. In this I have confirmed the experiments of Magendie, in 1822 and 1839, experiments which

he failed to repeat with success after that date, which were repeated in 1846 by Bernard, and later still by Schiff, but have never been repeated, so far as I am aware, in England or this country. In these experiments I have attempted to show nothing beyond the recurrent sensibility and its derivation from the posterior, or sensory roots.

IV

HISTORICAL CONSIDERATIONS CONCERNING THE PROPERTIES OF THE ROOTS OF THE SPINAL NERVES

Published in the "Quarterly Journal of Psychological Medicine" for October,
1868.

At the time when the functions of the nerves given off from the spinal cord began to be understood by physiologists, there was much discussion in regard to the claims of different observers to the honor of the discovery of the different properties of their anterior and posterior roots. Alexander Walker,* Sir Charles Bell † and Herbert Mayo, ‡ in England, all claimed a share, more or less considerable, in this great discovery; and in France, Magendie* professed to have been the first to demonstrate this important fact by direct experiment.

* Walker, "The Nervous System, anatomical and physiological: in which the functions of the various parts of the brain are for the first time assigned, and to which is prefixed some account of the author's earliest discoveries, of which the more recent doctrine of Bell, Magendie, etc., is shown to be at once a plagiarism, an inversion, and a blunder, associated with useless experiments, which they have neither understood nor explained." London, 1844, p. 50, *et seq.*

† Bell, "The Nervous System of the Human Body: as explained in a series of papers read before the Royal Society of London." London, 1844, p. 13, *et seq.*

Shaw, "Narrative of the Discoveries of Sir Charles Bell in the Nervous System." London, 1839.

‡ Mayo, "Outlines of Human Physiology." London, 1827, p. 240.

* Magendie, "Expériences sur les fonctions des racines des nerfs rachidiens,"—*Journal de physiologie*. Paris, 1822, tome ii., p. 276; et "Expériences sur les fonctions des racines des nerfs qui naissent de la moelle épinière." *Ibid.*, p. 366.

Magendie et Desmoulins, "Anatomie des systèmes nerveux des animaux à vertèbres." Paris, 1825, tome ii., p. 777.

Magendie, "Précis élémentaire de physiologie." Deuxième édition. Paris, 1825, tome i., pp. 167 and 216.

—— "Note additionnelle aux deuxième mémoire sur les nerfs de la face,"—*Journal de physiologie*. Paris, 1830, tome x., p. 189.

—— "Leçons sur les fonctions et les maladies du système nerveux." Paris, 1841, tome i., p. 64.

The pretensions of Walker and of Mayo are easily disposed of. Walker, who was undoubtedly the first to distinctly state, in 1809, that one of the roots of the nerves was for sensation, while the other presided over movements, did not support his theory by any facts or experiments and was led into the error of supposing that the anterior roots were sensitive and the posterior were motor, precisely the reverse of what was proved to be the case by the subsequent experiments of Magendie. Walker, in his work, ridicules the idea of studying the functions of the body by experiments on living animals; yet he details an experiment, "the only operation on a living animal which he ever has performed, or ever will perform," in which he exposed the roots of the spinal nerves in a frog and found "that irritation of the anterior roots caused motion, and irritation of the posterior caused little or none." * Inasmuch as Walker claimed in his publications, as late as 1844, that he had always considered the posterior roots as motor and the anterior as sensitive, it does not seem that he has any well-founded title to the discovery of the real properties of these nerves. The claims of Mayo are even more indefinite. He simply states, long after the publication of the experiments of Magendie, that "the remarkable analogy which exists between the fifth nerve and the spinal nerves, led me to suppose that the two roots of the spinal nerves had the same discrepancy of function with the two roots of the fifth; and that the ganglionic portion might belong to sensation, the smaller anterior portion to volition." †

All discussion, therefore, relative to priority in the discovery of the true functions of the roots of the nerves is confined to the claims of Bell and of Magendie. The experiments of Müller ‡ and others were all made after 1822, the date of the first publication of the experiments of Magendie in the "Journal de physiologie."

In nearly every treatise on physiology published since 1822 and in almost all works on the nervous system subsequent to that date, the great discovery of the distinct seat of motion and sensation in the spinal nerves is ascribed to

* Walker, *Op. cit.*, p. 18.

† Mayo, *Loc. cit.*

‡ Müller, "Physiologie du système nerveux." Paris, 1840, tome i., p. 85, *et seq.*; and "Manuel de physiologie." Paris, 1851, tome i., p. 598, *et seq.* The experiments of Müller were first published in 1831.

Sir Charles Bell. The name of Magendie is seldom mentioned in this connection, even in France; and his discoveries are supposed to relate chiefly to the seat of sensation and motion in the different columns of the spinal cord.

Before discussing the real claims of Bell and Magendie, it may not be uninteresting to review the statements in some of the more common works by English, German and French authors. Todd and Bowman* say that "it can not be denied that the endowment of the roots was discovered by Bell;" Carpenter† says "that the merit of this discovery is almost entirely due to Sir Charles Bell;" Kirkes‡ makes the same statement; Bostock* associates the names of Bell and Magendie but says that the experiments of Bell were clearly antecedent to those of Magendie; but Elliotson,|| who had evidently consulted carefully the literature of the subject, distinctly asserts that Bell had no idea that the anterior roots of the spinal nerves were motor and the posterior roots sensory, before the publication of Magendie's experiments in 1822; and he ascribes the whole honor of the discovery to Magendie. So far as I am aware, Elliotson is the only English writer, except Walker and Mayo, who themselves laid claim to the discovery, who does not ascribe the whole honor to Bell.⁴

In all the German works which I have examined, the credit of the discovery is given to Bell. Reference has already been made to the work of Müller on the nervous system,⁵ and his manual of physiology.⁶ The discovery is also unreservedly ascribed to Bell by Valentin,⁷ by Volkmann⁸ and by Budge.**

* Todd and Bowman, "The Physiological Anatomy and Physiology of Man." Philadelphia, 1857, p. 274.

† Carpenter, "Principles of Human Physiology." Philadelphia, 1853, p. 651.

‡ Kirkes, "Manual of Physiology." Philadelphia, 1857, p. 327.

* Bostock, "An Elementary System of Physiology." London, 1824, vol. i., p. 281.

|| Elliotson, "Human Physiology." London, 1840, p. 465.

I should also except the author of a review in the "London Medical and Physical Journal" for 1829. This review will be referred to hereafter.

⁴ *Op. cit.*, p. 85.

⁵ *Op. cit.*, p. 598.

⁶ Valentin, "Lehrbuch der Physiologie des Menschen." Braunschweig, 1844, Band ii., S. 627.

⁷ Volkmann, in "Wagner's Handwörterbuch der Physiologie." Braunschweig, 1844, Band ii., S. 558.

** Budge, "Lehrbuch der Speciellen Physiologie des Menschen." Leipzig, 1862, S. 623.

The most interesting bibliographical researches on this subject are in connection with the French treatises on physiology and on the nervous system. In 1816 Magendie published his "*Précis élémentaire de physiologie*," which, in its arrangement and the general method of considering the subject, has served as the model of the best works on physiology which have appeared since that date. In his various publications already referred to, and in the second edition of the "*Précis élémentaire*," published in 1825, as well as in subsequent editions of the same work, Magendie formally lays claim to the credit of the discovery of the functions of the roots of the nerves; and in the "*Journal de physiologie*" * he gives full credit to Sir Charles Bell for his observations, quoting, in the original, the account of the only experiment performed by Bell; and yet, with one or two exceptions, all the French works which treat of the subject seem to regard Sir Charles Bell as the real discoverer. The author to whom I particularly refer as the exception is Vulpian, who has lately published a very interesting work on the nervous system. Vulpian does not distinctly state that he has consulted the original memoir printed by Bell in 1811, but he seems to appreciate so fully the state of the question that the present review would have been rendered unnecessary had I not been enabled to produce an exact reprint of the original memoir † (of the existence of which Vulpian does not seem to be aware), and from this to confirm fully the statements in regard to the priority in this great discovery. Vulpian ‡ recognizes fully the injustice which Magendie has so long received, and exposes, also, the unwarrantable alterations which Bell has made in a paper originally published in the "*Philosophical Transactions*" in 1821, and reprinted subsequently in 1844.* In the reprint of this paper Bell has not hesitated to so modify his language as to make his remarks correspond with the facts discovered by Magendie in 1822, giving to the reader the impression that he held these opinions as early as 1821.

* Tome x., p. 370.

† "*Documents and Dates of Modern Discoveries in the Nervous System.*" London, John Churchill, 1839, p. 37, *et seq.*

‡ Vulpian, "*Leçons sur la physiologie générale et comparée du système nerveux.*" Paris, 1866, pp. 109 et 127.

* Bell, "*The Nervous System of the Human Body: as explained in a series of papers read before the Royal Society of London.*" London, 1844, p. 33.

Longet in his work on the nervous system says: "We see that, without having absolutely demonstrated it, Ch. Bell suspected that the rôle of the posterior roots relates to sensibility." * In this work Longet quotes from Bell's memoir of 1811 reprinted in the "Documents and Dates of Modern Discoveries in the Nervous System." The same passage occurs in Longet's "Traité de physiologie," but the quotations are here made from the English and the French editions of the work of Mr. Shaw.† Among the other French authors who ascribe the discovery of the properties of the roots of the spinal nerves to Ch. Bell, may be mentioned Béclard,‡ Flourens,* Foville|| and Gratiolet.ª All of these authors, with enthusiasm, ascribe to Charles Bell the great discovery which I shall show belongs to Magendie.

I

REVIEW OF THE CLAIMS OF SIR CHARLES BELL TO THE
DISCOVERY OF THE PROPERTIES OF THE ROOTS OF THE
SPINAL NERVES, AS SHOWN BY HIS WRITINGS, AND BY
THE NARRATIVE OF HIS DISCOVERIES, BY MR. SHAW

The original memoir by Sir Charles Bell, entitled "Idea of a New Anatomy of the Brain," which was printed in 1811,¶ is now almost inaccessible. It was printed for private distribution and it is said that the number of copies

* Longet, "Anatomie et physiologie du système nerveux de l'homme et des animaux vertébrés." Paris, 1832, tome i., p. 28.

† Longet, "Traité de physiologie." Paris, 1860, p. 172.

‡ Béclard, "Traité élémentaire de physiologie humaine." Paris, 1859, p. 761.

* Flourens, "Recherches expérimentales sur les propriétés et les fonctions du système nerveux dans les animaux vertébrés." Paris, 1842, p. 13. Flourens, in his Memoir of Magendie read at the Academy of Sciences, soon after the death of this great physiologist, in 1855, again ascribes the credit of the discovery of the different properties of the roots of the spinal nerves to Charles Bell. A translation of this memoir is published in the Smithsonian Report for 1866, p. 91, *et seq.*

|| Foville, "Traité complet de l'anatomie, de la physiologie et de la pathologie du système nerveux cérébro-spinal (1ère partie) anatomie." Paris, 1844, p. 493.

ª Leuret et Gratiolet, "Anatomie comparée du système nerveux considéré dans ses rapports avec l'intelligence." Paris, 1839-1857, tome ii., p. 330.

¶ In a paper read before the Medico-Chirurgical Society, in April, 1822, Mr. J. Shaw gives the date of the first paper by Charles Bell as 1809. This error is quoted into many reviews and other publications, but it has been corrected by Bell himself and by Mr. Shaw. (Alexander Shaw's "Narrative of the Discoveries of Sir Charles Bell in the Nervous System," London, 1830, p. 14.)

was only one hundred.* From the writings of various authors who have discussed the claims of Bell and of Magendie, it appears that few have had the opportunity of consulting the original paper. It is, of course, frequently referred to by Bell himself, and by Mr. Shaw, his brother-in-law. Magendie speaks of having obtained a copy of this work and gives a quotation from it in the "Journal de physiologie," † Müller refers to the original paper but does not definitely state that he has had the opportunity of consulting it.‡ In a review published in the "London Medical and Physical Journal" in 1829, it is distinctly stated that the original paper was consulted; * and in a reply to this review by a pupil of Charles Bell, published in the same Journal, in 1830, reference is again made to the original tract.|| A later writer in the "British and Foreign Medico-Chirurgical Review" assumes to have compared the reprint, already referred to, with the original paper.[^] With these exceptions, no author, so far as I know, has consulted the original document; and the claims of Charles Bell to the discovery are based upon quotations from the pamphlet of 1811, made by himself and by Mr. Shaw, which have been copied into nearly all works treating of the physiology of the nervous system. Writers on this subject have thus been forced to get their ideas of the claims of Charles Bell from his later publications, particularly his work on the nervous system, ¶ which has been very widely circulated and has passed through several editions. I have before me a work, apparently very little known, entitled "Documents and Dates of Modern Discoveries in the Nervous System," published in London, in 1839, by John Churchill. This volume contains a reprint of the original paper of Charles Bell, entire. So far as I have been able to compare this reprint with the

* Vulpian, "Leçons sur la physiologie générale et comparée du système nerveux," Paris, 1866, p. 109.

† *Op. cit.*, tome ii., p. 370.

‡ Müller, "Physiologie du système nerveux," Paris, 1840, tome i., p. 85.

* "The London Medical and Physical Journal," 1829, vol. lxii., p. 525.

|| *Ibid.*, 1830, vol. lxiii., p. 40. This writer refers to the tract as printed in 1809.

[^] "The British and Foreign Medico-Chirurgical Review," London, 1840, vol. ix., p. 98.

¶ Bell, "The Nervous System of the Human Body," third edition, London, 1844.

quotations from the original by Bell and by Shaw, it has proved to be entirely accurate. Its accuracy is also attested by the writer in the "Medico-Chirurgical Review," already referred to. It does not appear that this volume is referred to by any physiological writers except Longet;* and it is a matter of surprise that this distinguished author, if he has carefully read the memoir of Charles Bell, can refrain from giving to Magendie full credit for his brilliant discovery. In his work on physiology,† Longet quotes the paper of Bell from the "Narrative" of Mr. Shaw, and says nothing about the "Documents and Dates." It is all the more surprising that the claims of Magendie should not be recognized in France, when an English writer, Elliotson, had already rendered him full justice, which was also given him, in 1829, by a reviewer in the "London Medical and Physical Journal," the author of the review here attributing "this great discovery entirely to Magendie."‡

With all the publications by Bell and Magendie before us, it would seem that now, when the acrimony of controversy has subsided, we should be able to settle the claims of each of these physiologists to the discovery under consideration. I shall abstain from reviewing the discussions of this question which took place soon after the publication of Magendie's experiments, and proceed to study carefully the various publications on this subject, by Bell and Magendie, beginning with the memoir printed in 1811.

VIEWS OF SIR CHARLES BELL, IN 1811, CONCERNING THE
PROPERTIES OF THE ROOTS OF THE SPINAL NERVES,
TAKEN FROM HIS "IDEA OF A NEW ANATOMY OF THE
BRAIN"

Almost all the quotations which I shall make from this remarkable pamphlet are to be found in Shaw's "Narrative" of Bell's discoveries, a work which is sufficiently common and accessible and which certainly presents the claims of Bell in the most favorable light possible. I refer

* Longet, "Anatomie et physiologie du système nerveux de l'homme et des animaux vertébrés," Paris, 1842, tome i., p. 27.

This reprint of Bell's original memoir is distinctly referred to by Bernard in his "Rapport sur le progrès et la marche de la physiologie générale en France," Paris, 1867, p. 155, which has appeared since this review was written.

† Longet, "Traité de physiologie," Paris, 1860, tome ii., p. 172.

‡ *Loc. cit.*, p. 532.

the reader to this work to show that nothing is omitted in the following quotations which has an important bearing on the subject under consideration.

After a short notice of the then prevailing opinions concerning the structure and functions of the nerves and the encephalon, Bell proceeds to give a general statement of his views, as follows:

"In opposition to these opinions, I have to offer reasons for believing that the cerebrum and cerebellum are different in function as in form; that the parts of the cerebrum have different functions; and that the nerves which we trace in the body are not single nerves possessing various powers, but bundles of different nerves, whose filaments are united for convenience of distribution, but which are distinct in office, as they are in origin, from the brain.

"That the external organs of the senses have the matter of the nerves adapted to receive certain impressions, while the corresponding organs of the brain are put in activity by other external excitement. That the idea or perception is according to the part of the brain to which the nerve is attached, and that each organ has a certain limited number of changes to be wrought upon it by the external impression.

"That the nerves of sense, the nerves of motion, and the vital nerves, are distinct through their whole course, though they seem sometimes united in one bundle; and that they depend for their attributes on the organs of the brain to which they are severally attached.

"The view which I have to present will serve to show why there are divisions, and many distinct parts in the brain; why some nerves are simple in their origin and distribution, and others intricate beyond description. It will explain the apparently accidental connection between the twigs of nerves. It will do away with the difficulty of conceiving how sensation and volition should be the operation of the same nerve at the same moment. It will show how a nerve may lose one property and retain another; and it will give an interest to the labors of the anatomist in tracing the nerves"—(pp. 39, 40).

This extract simply shows that Bell entertained the opinion prevalent at that day, that all the nerves derived their properties from the encephalon. The new idea which he advances is, that the nerves are to be divided into nerves of motion, nerves of sensation and vital nerves, which last were at that time supposed to be the nerves which presided over the organic functions. The theoretical division of the nervous fibres into motor and sensory had been made by Alexander Walker in 1809; * and Willis held the opin-

* *Loc. cit.*

ion that the cerebellum, from which Bell supposed that the "vital nerves" were derived, presided over the functions of organic life. These ideas, therefore, cannot be claimed as original.

After some general considerations concerning the structure and probable function of different parts of the nervous system, the following experiments are detailed:

"In thinking of this subject, it is natural to expect that we should be able to put the matter to proof by experiment. But how is this to be accomplished, since any experiment direct upon the brain itself must be difficult, if not impossible? I took this view of the subject. The medulla spinalis has a central division, and also a distinction into anterior and posterior fasciculi, corresponding with the anterior and posterior portions of the brain. Further, we can trace down the crura of the cerebrum into the anterior fasciculus of the spinal marrow, and the crura of the cerebellum into the posterior fasciculus. I thought that here I might have an opportunity of touching the cerebellum, as it were, through the posterior portion of the spinal marrow, and the cerebrum by the anterior portion. To this end I made experiments, which, though they were not conclusive, encouraged me in the view I had taken.

"I found that injury done to the anterior portion of the spinal marrow convulsed the animal more certainly than injury done to the posterior portion; but I found it difficult to make the experiment without injuring both portions.

"Next, considering that the spinal nerves have a double root, and being of opinion that the properties of the nerves are derived from their connections with the parts of the brain, I thought I had an opportunity of putting my opinion to the test of experiment, and of proving at the same time that nerves of different endowments were in the same cord, and held together by the same sheath.

"On laying bare the roots of the spinal nerves, I found that I could cut across the posterior fasciculus of nerves, which took its origin from the posterior portion of the spinal marrow, without convulsing the muscles of the back; but that on touching the anterior fasciculus with the point of the knife, the muscles of the back were immediately convulsed. Such were my reasons for concluding that the cerebrum and the cerebellum were parts distinct in function, and that every nerve possessing a double function obtained that by having a double root. I now saw the meaning of the double connection of the nerves with the spinal marrow; and also the cause of that seeming intricacy in the connections of the nerves throughout their course, which were not double in their origin.

"The spinal nerves being double, and having their roots in the spinal marrow, of which a portion comes from the cerebrum and a portion from the cerebellum, they convey the attributes of both grand divisions of the brain to every part; and therefore the distribution of such nerves is simple, one nerve supplying its distinct part"—(pp. 50-52).

The above quotation embodies all the experiments detailed by Bell in his first essay. From the account of these experiments given by Vulpian, it would not seem that he had consulted the original work. Vulpian speaks of the first experiment on the spinal cord as performed upon a rabbit recently killed. No such statement is made in the original. He also speaks of the experiment upon the roots of the nerves as made upon a living animal.* This does not appear in the original. On the contrary, Bell speaks of cutting across the posterior roots (p. 51) without "convulsing the muscles of the back," and has nothing to say about the sensibility, which certainly would have been manifested if the operation had been performed on a living animal.

A careful review of the last quotation, which is also made in full by Shaw, will give a clear idea of the real opinion of Bell concerning the different properties of the roots of the nerves. He evidently regards the anterior fasciculi of the cord as prolongations of the *crura cerebri*; and the posterior fasciculi as prolongations of the *crura cerebelli*; and he found that injury to the anterior portion of the cord produced convulsions "more certainly" than injury done to the posterior portion. He next assumes that the double roots of the spinal nerves receive their properties from their connections with different parts of the brain (the cerebrum and cerebellum); and his experiments on the roots of the nerves agreeing in every respect with the experiments upon the anterior and posterior fasciculi of the cord, he concludes that the cerebrum and cerebellum, and consequently the different roots of the spinal nerves, are parts distinct in function.

It remains now to see what distinct functions are ascribed to the cerebrum and cerebellum, and consequently to the nerves proceeding from these parts. This is clearly indicated in the following quotation:

"The cerebellum, when compared with the cerebrum, is simple in its form. It has no internal tubercles or masses of cineritious matter in it. The medullary matter comes down from the cineritious cortex, and forms the *crus*; and the *crus* runs into union with the same process from the cerebrum; and they together form the *medulla spinalis*, and are continued down into the spinal marrow;

* Vulpian, *Op. cit.*, p. III.

and these crura or processes afford double origin to the double nerves of the spine. The nerves proceeding from the *crus cerebelli* go everywhere (in seeming union with those from the *crus cerebri*); they unite the body together, and control the actions of the bodily frame; and especially govern the operation of the viscera necessary to the continuance of life.*

"In all animals having a nervous system, the cerebellum is apparent, even though there be no cerebrum. The cerebrum is seen in such tribes of animals as have organs of sense, and it is seen to be near the eyes, a principal organ of sense; and sometimes it is quite separate from the cerebellum.

"The cerebrum I consider as the grand organ by which the mind is united to the body. Into it all the nerves from the external organs of the senses enter; and from it all the nerves which are agents of the will pass out"—(pp. 53, 54).

The above quotations complete the history of Sir Charles Bell's ideas in regard to the functions of the roots of the nerves. The posterior roots are supposed to "unite the body together, and control the actions of the bodily frame; and especially govern the operation of the viscera necessary to the continuance of life." The anterior roots convey to the cerebrum impressions "from the external organs of the senses," and are the nerves by which the agents of the will pass out. It is true that the language is not very clear or strictly scientific according to our present ideas, but it must be evident to every one that Bell regarded the anterior roots as nerves of both motion and sensation, and the posterior roots as the so-called "vital" nerves. Indeed, Mr. Alexander Shaw, the most enthusiastic and persistent partisan of Bell, admits the uncertainty of Bell's statements concerning the seat of sensation in the nervous roots in the following passage: "Accordingly, that it is left in doubt by Sir Charles Bell, when he composed his 'Essay on the Brain' in 1811, whether the power of giving sensation belonged to the posterior root, must be admitted." † The quotation made above, which was omitted by Mr. Shaw, shows that this statement is not strictly correct. The question of sensibility of the posterior roots was not

* This important paragraph, in which the functions of the posterior roots of the nerves ("the nerves proceeding from the *crus cerebelli*") are distinctly assigned without a mention of any sensory property, is not quoted by Shaw; and this passage, which is nowhere contradicted, makes it evident that Bell knew nothing and discovered nothing of the properties of the sensory roots.

† Shaw, "Narrative of the Discoveries of Sir Charles Bell in the Nervous System." London, 1839, p. 46.

mentioned by Bell; and, far from being "left in doubt," another function was assigned.

The following quotation from Bell's work reiterates the supposed functions of the roots:

"The convex bodies, which are seated in the lower part of the cerebrum, and into which the nerves of sense enter, have extensive connection with the hemispheres on their upper part. From the medullary matter of the hemispheres, again, there pass down, converging to the crura, striæ, which is the medullary matter, taking upon it the character of a nerve; for, from the crura cerebri, or its prolongation in the anterior fasciculi of the spinal marrow, go off the nerves of motion.

"But with these nerves of motion, which are passing outward, there are nerves going inward; nerves from the surfaces of the body; nerves of touch; and nerves of peculiar sensibility, having their seat in the body or viscera. It is not improbable that the tracts of cineritious matter which we observe in the course of the medullary matter of the brain, are the seat of such peculiar sensibilities; the organs of certain powers which seem resident in the body"—(pp. 55, 56).

The above passage leaves no doubt that Bell thought that the nerves of motion, going off from the anterior fasciculi of the spinal marrow, contained filaments of sensation in the same sheath.

The last paragraph of the original memoir, which apparently contains the conclusions drawn by its author from his facts and experiments, should never have been omitted in quotations intended to give a correct idea of the views of Sir Charles Bell, as exemplified by this remarkable pamphlet. This, however, is not quoted by Mr. Shaw, or, so far as I can ascertain, by any other writer. This paragraph needs no comment, as it presents the views of the author more clearly than any other passage:

"From the cineritious matter, which is chiefly external, and forming the surface of the cerebrum; and from the grand centre of the medullary matter of the cerebrum, what are called the crura descend. These are fasciculated processes of the cerebrum, from which go off the nerves of motion, the nerves governing the muscular frame. Through the nerves of sense the sensorium receives impressions, but the will is expressed through the medium of the nerves of motion. The secret operations of the bodily frame, and the connections which unite the parts of the body into a system, are through the cerebellum and the nerves proceeding from it"—(p. 60).

It is not pretended that Charles Bell made any publication concerning the functions of the roots of the spinal

nerves between 1811 and 1821, when he read before the "Royal Society of London" a paper "On the nerves; giving an account of some experiments on their structure and functions, which lead to a new arrangement of the system." In this article, as it is printed in the "Philosophical Transactions," 1821, Part I., p. 398, *et seq.*, there is no indication that the author was aware of the true properties of the anterior and posterior roots. The claims of Bell to this discovery, then, rest entirely on the unpublished pamphlet of 1811; and the extracts I have given show conclusively that he attributed to the posterior roots properties which they do not possess, and gave to the anterior roots the properties both of motion and sensation.

The state of the question in 1811 may, then, be summed up in a very few words:

In 1809, Alexander Walker proposed the theory that one of the roots of the spinal nerves was for motion and the other for sensation. This was done on purely theoretical grounds; and Walker erred in supposing that the posterior roots were motor and the anterior sensory.*

In 1811, Sir Charles Bell advanced the views which I have already fully given; and to him is due the credit of having been the first to attempt to verify his theories by

* Walker states his theory of the distinct functions of the roots of the nerve in the following words:

"Thus, then, it is proven to us, that medullary action commences in the organs of sense; passes, in a general manner, to the spinal marrow, by the anterior fascicula of the spinal nerves, which are, therefore, nerves of sensation, and the connections of which with the spinal marrow or brain must be termed their spinal or cerebral terminations; ascends through the anterior columns of the spinal marrow, which are, therefore, its ascending columns; passes forward through the inferior fasciculi of the medulla oblongata, and then through the crura cerebri; extends forward, outward, and upward through the corpora striata; and reaches the hemispheres of the cerebrum itself. This precisely is the course of its ascent to the sensorium commune.

"From the posterior part of the medulla of the hemispheres, it returns by the thalami, passing backward, inward, and downward; flows backward in the fasciculi under the nates and testes; backward and upward through the processes cerebelli ad testes or anterior peduncles of the cerebellum; and thus reaches the medulla of the cerebellum itself.

"From the cerebellum it descends through the posterior columns of the spinal marrow, which are, therefore, its descending columns; and expands through the posterior fasciculi of all the nerves, which are, therefore, the nerves of volition, and the connection of which with the spinal marrow or brain must be termed their spinal or cerebellic origins. This precisely is the course of its descent from the sensorium commune toward the muscular system."—"Documents and Dates of Modern Discoveries in the Nervous System." London, 1839, p. 36.)

experiments. He was undoubtedly the first to operate upon the roots of the spinal nerves in an animal recently killed; but he was far from attributing to each root its proper function, which was done by Magendie in 1822.

REVIEW OF THE WRITINGS OF SIR CHARLES BELL SUBSEQUENT TO 1811, IN WHICH IT IS IMPLIED THAT HE DISCOVERED THE FUNCTIONS OF THE ROOTS OF THE SPINAL NERVES

All the credit which I have to give to Sir Charles Bell for advances in the anatomy and physiology of the spinal nerves must cease with the review of the pamphlet of 1811. In a memoir on the nerves of the head, read before the "Royal Society," July 12, 1821, more than a year before the publication of the experiments of Magendie, there is no mention of distinct motor and sensory roots of the spinal nerves or of distinct properties in different portions of the spinal cord. This paper was republished by Bell, after the publication of Magendie's observations, in a work on the nervous system; and it is this republication which is most accessible and most frequently referred to by physiological writers. The republication avowedly contains "some additional explanations;" but a careful comparison of it with the original shows that every portion of it that was susceptible of such verbal alteration has been modified to make it correspond with the discovery by Magendie. But at the same time, the impression received by the reader is that it is essentially the same as the memoir published in 1821. These alterations have been commented upon by Vulpian; but I propose to give some extracts from the two papers, side by side, showing how the unwarrantable verbal alterations in the reprint are calculated to give the impression that Bell was fully aware of the true seat of motion and sensation in the spinal cord and the spinal nerves, and had succeeded, by applying the same mode of investigation to the nerves of the brain, in demonstrating "that the principle in question held good equally with regard to them as with regard to the spinal nerves." *

* "This is claimed for Bell by his brother-in-law, Mr. Alexander Shaw, from whom the above passage in quotation marks is taken."—(Shaw, "Narrative of the Discoveries of Charles Bell in the Nervous System." London, 1839, p. 8.)

EXTRACTS FROM THE MEMOIRS OF SIR CHARLES BELL, PUBLISHED IN THE PHILOSOPHICAL TRANSACTIONS AND IN HIS WORK ON THE NERVOUS SYSTEM *

ON THE NERVES; GIVING AN ACCOUNT OF SOME EXPERIMENTS ON THEIR STRUCTURE AND FUNCTIONS, WHICH LEAD TO A NEW ARRANGEMENT OF THE SYSTEM. By Charles Bell, Esq., communicated by Sir Humphrey Davy, Bart., P. R. S. Read, July 12, 1821. Philosophical Transactions, London, 1821, Part I., p. 398, *et seq.*

ON THE NERVES; GIVING A VIEW OF THEIR STRUCTURE AND ARRANGEMENT, WITH AN ACCOUNT OF SOME EXPERIMENTS ILLUSTRATIVE OF THEIR FUNCTIONS. From the Philosophical Transactions, 1821, with some additional explanations. — The nervous system of the human body, as explained in a series of papers read before the Royal Society of London. By Sir Charles Bell, K. G. H., etc., etc. Third edition, London, 1844, p. 33, *et seq.*

ORIGINAL

OF THE TRIGEMINUS, OR FIFTH PAIR. In all animals that have a stomach, with palpi or tentacula to embrace their food, the rudiments of this nerve may be perceived; and always in the vermes, that part of their nervous system is most easily discerned which surrounds the œsophagus near the mouth. If a feeler of any kind project from the head of an animal, whether the antenna of a lobster or the trunk of an elephant, *it is a branch of this nerve which supplies sensibility to the member and animates its muscles. But this is only if it be a simple organ of feeling, and is not in its office connected with respiration.*

REPRINT

OF THE TRIGEMINUS, OR FIFTH PAIR, *the nerve of sensation and mastication.* In all animals that have a stomach, with palpi or tentacula to embrace their food, the rudiments of this nerve may be perceived; and always in the vermes, that part of their nervous system is most easily discerned which surrounds the œsophagus near the mouth. If a feeler of any kind project from the head of an animal, whether the antenna of a lobster or the trunk of an elephant, *it is by a branch of this nerve that it is supplied with sensibility. But if it be not merely a simple organ of feeling, but in its office connected with respiration, another nerve is added. The trunk of the elephant is not a simple feeler; it is a tube through which it respire, and therefore it has a different nerve superadded, to move it as a hand, and to expand it in the act of inspiration.*

* The passages that have been altered are printed in italics.

From the nerve which comes off from the anterior ganglion of the leech, and which supplies its mouth, we may trace up through the gradations of animals a nerve of taste and mastication, until we arrive at the complete distribution of the fifth, or trigeminus, in man. Here in the highest link, as in the lowest, the nerve is subservient to the same functions. *It is the nerve of taste and of the salivary glands; of the muscles of the face and jaws, and of common sensibility. It comes off from the base of the brain in so peculiar a situation, that it alone, of all the nerves of the head, receives roots both from the medullary process of the cerebrum and the cerebellum.* A ganglion is formed upon it near its origin, though some of its filaments pass on without entering into the ganglion. Before passing out of the skull, the nerve splits into three great divisions, which are sent to the face, jaws, and tongue. Its branches go minutely into the skin, and enter into all the muscles, and they are especially profuse to the muscles which move the lips upon the teeth—(pp. 409, 410).

From the nerve which comes off from the anterior ganglion of the leech, and which supplies its mouth, we may trace up through the gradations of animals a nerve of taste and mastication, until we arrive at the complete distribution of the fifth, or trigeminus, in man. Here in the highest link, as in the lowest, the nerve is subservient to the same functions. *It is the nerve of the muscles of the jaws, and of common sensibility, of taste, and of the salivary glands. It comes off from the base of the brain in so peculiar a situation, that it alone, of all the nerves of the head, receives roots both from the column of sensibility and that of motion.* A ganglion is found upon it near its origin, though some of its filaments pass on without entering into the ganglion. Before passing out of the skull, the nerve splits into three great divisions, which are sent to the face, jaws, and tongue. Its branches go minutely into the skin, and enter into all the muscles, and they are especially profuse to the lips—(pp. 47, 48).

OF THE RESPIRATORY NERVE OF THE FACE, BEING THAT WHICH IS CALLED THE PORTIO DURA OF THE SEVENTH.

In this extensive distribution, the nerve penetrates to all the muscles of the face; *muscles supplied also with the branches of the fifth pair. Its branches penetrate to the skin accompanying the minute vessels of the cheek—(p. 411).*

OF THE PORTIO DURA OF THE SEVENTH NERVE—THE MOTOR AND RESPIRATORY NERVE OF THE FACE.

In this extensive distribution, the nerve penetrates to all the muscles of the face; *muscles supplied also with the sensitive branches of the fifth pair—(p. 50).*

EXPERIMENTS ON THE NERVES
OF THE FACE.

An ass being thrown, and its nostrils confined for a few seconds, so as to make it pant and forcibly dilate the nostrils at each inspiration, the portio dura was divided on one side of the head; the motion of the nostril of the same side instantly ceased, while the other nostril continued to expand and contract in unison with the motions of the chest.

On division of this nerve, the animal will give no sign of pain; or in no degree equal to what results from dividing the fifth nerve.

An ass being tied and thrown, and the superior maxillary branch of the fifth nerve exposed, touching this nerve gave acute pain. It was divided, but no change took place in the motion of the nostril; the cartilages continued to expand regularly in time with the other parts, which combine in the act of respiration. If the same branch of the fifth be divided on the opposite side, and the animal let loose, he will not pick up his corn; the power of elevating and projecting the lip, as in gathering food, was lost. He will press the mouth against the ground, and at length will lick the oats from the ground with his tongue. In my first experiment, the loss of motion of the lips was so obvious, that it was thought a useless cruelty to cut the other branches of the fifth—(pp. 412, 413).

EXPERIMENTS ON THE NERVES
OF THE FACE, with a view to ascertain the uses of the portio dura.

If an ass be thrown, and the portio dura be cut across where it emerges upon the face, before the ear, all the muscles of the face, except those of the jaws, will be paralyzed. If its nostrils be confined for a few seconds, so as to make it pant and forcibly dilate the nostrils at each inspiration, and if the portio dura be now divided on one side of the head, the motion of the nostril of the same side will instantly cease, while the other nostril will continue to expand and contract in unison with the motions of the chest.

On division of this nerve, the animal will give no sign of pain; or in no degree equal to what results from dividing the fifth nerve.

If an ass be tied and thrown, and the superior maxillary branch of the fifth nerve exposed, touching this nerve gives acute pain. When it is divided, no change takes place in the motion of the nostril; the cartilages continue to expand regularly in time with the other parts which combine in the act of respiration; but the sensibility is entirely lost. If the same branch of the fifth be divided on the opposite side, and the animal let loose, the parts will be deprived of sensibility, and he will not pick up his corn: the power of elevating and projecting the lip, as in gathering food, will appear to be lost. He will press the mouth against the ground, and at length lick the oats from the ground with his tongue. In my first experiments the loss of sensibility of the lips was so obvious, that it

From these facts we are entitled to conclude, that the portio dura of the seventh is the respiratory nerve of the face; that the motions of the lips, the nostrils, and the velum palati, are governed by its influence, when the muscles of these parts are in associated action with the other organs of respiration—(p. 414).

OF THE FUNCTIONS OF THE TRIGEMINUS, OR FIFTH NERVE, AS ILLUSTRATED BY THESE EXPERIMENTS.

Independently of the difference of sensibility in these nerves, there was exhibited, in all these experiments, a wide distinction in their powers of exciting the muscles. The slightest touch of the portio dura, or respiratory nerve, convulsed the muscles of the face, whilst the animal gave no sign of pain. By means of the branches of the fifth nerve, *it was more difficult to produce any degree of action in the muscles, although, as I have said, touching the nerve gave great pain*—(p. 58).

was thought a useless cruelty to cut the other branches of the fifth—(p. 52).

From these facts we are entitled to conclude, that the portio dura of the seventh *is the nerve of motion to the muscles of the forehead, eyebrow, eyelids, nostril, lips, and ear; that is, to all the muscles of the face except those of mastication—that it is the respiratory nerve of the face; that the motions of the lips, the nostrils, and the velum palati, are governed by its influence, when the muscles of these parts are in associated action with the other organs of respiration*—(p. 54).

OF THE FUNCTIONS OF THE TRIGEMINUS, OR FIFTH NERVE.

Independently of the difference of sensibility in these nerves, there was exhibited, in all these experiments, a wide distinction in their powers of exciting the muscles. The slightest touch of the portio dura, or respiratory nerve, convulsed the muscles of the face, whilst the animal gave no sign of pain. By means of the branches of the fifth nerve, *it was not possible to excite the muscles, if the trunk of the nerve were divided behind the part bruised; that is to say, if the communication with the sensorium were cut off*—(p. 58).

The paper from which the above extracts are made does not treat directly of the spinal nerves, but many passages are so worded in the reprint as to make it appear that its author recognized fully the distinction between the motor

and the sensory nerves throughout the system; and, as before remarked, it has been referred to by Shaw and others as evidence that these facts were well known before the publication of Magendie's experiments. In republishing a paper of this kind, the author undoubtedly had a right to make such additional explanations and such corrections as might be demanded by the advanced state of knowledge on the subject; but such alterations should have been so introduced as to be distinguishable from the original matter. Many additions, not bearing on the subject under consideration, have not been quoted; * and I have noted some unimportant alterations so as not to destroy the sense of the extracts; but a careful comparison of some of the passages which have been put side by side will make it evident that most of Sir Charles Bell's definite knowledge regarding the seat of motion and sensation in the nervous system was acquired after the first publication in the "Philosophical Transactions."

In the first extract, in speaking of a branch of the fifth, it will be seen that Bell confounds the two properties of motion and sensation; but he corrects this error in the reprint. He again speaks of this nerve as receiving roots from the medullary process of the cerebrum and the cerebellum; which, in the reprint, he calls "the column of sensibility and that of motion." In the first publication he calls the portio dura simply the "respiratory nerve of the face;" and in the reprint he has modified his phraseology, and speaks of it as the "motor and respiratory nerve of the face." In another place he details an experiment in which the superior maxillary branch of the fifth was divided in an ass; and in the reprint he states that sensibility was entirely lost, etc., but does not mention this in his original paper. He also says, in the same connection, that after this operation "the loss of motion of the lips was so obvious," etc., and in the reprint he has it that "the loss of sensibility of the lips was so obvious." A careful study of the first memoir will show that he never made correct applications of the terms motor and sensory with reference to different

* The alterations from the original publication in the "Philosophical Transactions" are much more extensive in the late editions of the work on the nerves than in the previous issues. In an edition reprinted in this country (Washington, 1833) the corrections are much fewer.

portions of the nervous system; and that this memoir of 1821 added nothing, as regards the discovery of the functions of the roots of the nerves, to the paper printed in 1811.*

II

REVIEW OF THE CLAIMS OF MAGENDIE TO THE DISCOVERY OF THE DISTINCT PROPERTIES OF THE ROOTS OF THE SPINAL NERVES

The first publications of Magendie concerning the anatomy and the functions of different portions of the nervous system appeared in the "Journal de physiologie," in 1821. In the first volume of this journal is a notice of the researches of Charles Bell on the nerves of the face, with an account of the observations of Mr. Shaw on the same subject.† Magendie here states that he repeated the experiments of Bell with MM. Shaw and Dupuy at Alfort.‡ Magendie had not at that time received the memoir of Bell; but in a succeeding number of the Journal he gives a full analysis of it.* In this number, also, he speaks of having repeated the experiments. In the same Journal follows a translation of the experiments of Mr. Shaw.|| In none of these publications is there any allusion to the properties of the anterior and posterior roots of the spinal nerves, nor is there any evidence that either Bell, Shaw or Magendie knew anything about the distinct seat of motion and sensation in the spinal cord and the spinal nerves.△

* A paper by Mr. John Shaw, in the "Medico-Chirurgical Transactions," in June, 1822, some months before Magendie's experiments were published, is said to contain an account of Bell's views of the nerves. The statements here, however, are no more definite than the quotations which I have made from Bell's original writings.

† "Recherches anatomiques et physiologiques sur le système nerveux;" par M. Charles Bell.—"Journal de physiologie," Paris, 1821, tome i., p. 384, *et seq.*

‡ *Loc. cit.*, p. 387.

* "Suite des recherches anatomiques et physiologiques sur le système nerveux," par M. Bell.—"Journal de physiologie," Paris, 1822, tome ii., p. 66, *et seq.*

|| "Expériences sur le système nerveux;" par M. Shaw. Extrait et traduit de l'Anglais par M. Cairns.—"Journal de physiologie," Paris, 1822, tome ii., p. 77, *et seq.*

△ In the same volume of the Journal (p. 363), Magendie gives an account of Bell's observations on the respiratory nerves of the chest, which were presented to the "Royal Society," May 2, 1822.

In August, 1822 Magendie published his first experiments on the functions of the roots of the spinal nerves.* Unlike any of the experiments performed by Bell on the spinal nerves, these were made upon living animals. The spinal canal was opened, and the cord, with the roots of the nerves, exposed. The posterior roots of the lumbar and sacral nerves were then divided upon one side and the wound united with sutures. The result of this observation was as follows: †

"I thought at first that the limb corresponding to the divided nerves was entirely paralyzed; it was insensible to pricking and to the most severe pinching, it also appeared to me to be motionless; but soon, to my great surprise, I saw it move in a very marked manner, although the sensibility was still entirely extinct. A second, a third experiment, gave me exactly the same result; I commenced to regard it as probable that the posterior roots of the spinal nerves might have functions different from the anterior roots, and that they were more particularly devoted to sensibility." ‡

The experiments in which the anterior roots were divided were no less striking:

"As in the preceding experiments, I only made the division upon one side, in order to have a term of comparison. One can conceive with what curiosity I followed the effects of this division; they were not at all doubtful, the limb was completely motionless and flaccid, while it preserved a marked sensibility. Finally, that nothing should be neglected, I divided at the same time the anterior and the posterior roots; then followed absolute loss of sensation and of motion."*

* "Expériences sur les fonctions des racines des nerfs rachidiens;" par F. Magendie.—"Journal de physiologie," Paris, 1822, tome ii., p. 276, *et seq.*

† The original of the important passages quoted from Magendie is given in foot-notes, and the translation into English is as nearly literal as possible.

‡ "Je crus d'abord le membre correspondant aux nerfs coupés, entièrement paralysé; il était insensible aux piqûres et aux pressions les plus fortes, il me paraissait aussi immobile; mais bientôt, à ma grande surprise, je le vis se mouvoir d'une manière très apparente, bien que la sensibilité y fût toujours tout-à-fait éteinte. Une seconde, une troisième expérience, me donnèrent exactement le même résultat; je commençais à regarder comme probable que les racines postérieures des nerfs rachidiens pourraient bien avoir des fonctions différentes des racines antérieures, et qu'elles étaient plus particulièrement destinées à la sensibilité."—"Journal de physiologie," Paris, 1822, p. 277.)

* "Comme dans les expériences précédentes, je ne fis la section que d'un seul côté d'avoir un terme de comparaison. On conçoit avec quelle curiosité je suivis les effets de cette section; ils ne furent point douteux, le membre était complètement immobile et flasque, tandis qu'il conservait une sensibilité non équivoque. Enfin, pour ne rien négliger, j'ai coupé à la fois les racines antérieures et les postérieures; il y a eu perte absolue de sentiment et de mouvement."—(*Ibid.*, p. 278.)

From these experiments Magendie drew the following conclusions:

"I am following out my researches, and shall give a more detailed account of them in the following number; it is sufficient for me to be able to announce at present as positive, that the anterior and the posterior roots of the nerves which arise from the spinal cord have different functions, that the posterior seem more particularly devoted to sensibility, while the anterior seem more especially connected with motion." *

In the second note, published in the same volume of the "Journal de physiologie," Magendie exposed and irritated the two roots of the nerves, with the following results:

"I commenced by examining in this regard the posterior roots, or the nerves of sensibility. The following is the result which I observed: on pinching, pulling, or pricking these roots, the animal manifested pain; but this was not to be compared as regards intensity with that which was developed if the spinal cord was touched, even lightly, at the point of origin of the roots. Nearly every time that the posterior roots were thus stimulated, contractions were produced in the muscles to which the nerves were distributed; these contractions, however, are not well marked, and are infinitely more feeble than when the cord itself is touched. When, at the same time, a bundle of the posterior root is cut, there is produced a movement in totality in the limb to which the bundle is distributed.

"I repeated the same experiments on the anterior roots, and I obtained analogous results, but in an opposite sense; for the contractions excited by the contusion, the pricking, etc., are very forcible, and even convulsive, while the signs of sensibility are hardly visible. These facts are, then, confirmatory of those which I have announced; only they seem to establish that sensation is not exclusively in the posterior roots, any more than motion in the anterior roots. Nevertheless, a difficulty may arise. When, in the preceding experiments, the roots had been cut, they were attached to the spinal cord. Might not the disturbance communicated to the cord be the real cause either of the contractions or of the pain which the animals experienced? To remove this doubt, I repeated the experiments after having separated the roots from the cord; and I must say that, except in two animals, in which I saw contractions when I pinched or pulled the anterior and posterior roots, in all the other instances I did not observe any sensible effect of irritation of the anterior or posterior roots thus separated from the cord." †

* "Je poursuis ces recherches et j'en donnerai un récit plus détaillé dans le prochain numéro; il me suffit de pouvoir avancer aujourd'hui comme positif, que les racines antérieures et les postérieures des nerfs qui naissent à la moelle épinière, ont des fonctions différentes, que les postérieures paraissent plus particulièrement destinées à la sensibilité, tandis que les antérieures semblent plus spécialement liées avec la mouvement."—(*Ibid.*, p. 279.)

† "J'ai commencé par examiner sous ce rapport les racines postérieures, ou les nerfs du sentiment. Voici ce que j'ai observé: en pinçant, tirant, et

Magendie then goes on to say that when he published the note in the preceding number of the Journal he supposed that he was the first who had thought of cutting the roots of the spinal nerves; but he was soon undeceived by a letter from Mr. Shaw, who stated that Bell had divided the roots thirteen years before. Magendie afterward received from Mr. Shaw a copy of Bell's essay (" Idea of a New Anatomy of the Brain"), and, as will be seen by the following extract, gave Bell full credit for all his observations.

" It is seen by this quotation from a work which I could not be acquainted with, inasmuch as it had not been published, that Mr. Bell, led by his ingenious ideas concerning the nervous system, was very near discovering the functions of the spinal roots; still the fact that the anterior are devoted to movement, while the posterior belong more particularly to sensation, seems to have escaped him; it is, then, to having established this fact in a positive manner that I must limit my pretensions." *

Such are the experiments by which the properties of the roots of the spinal nerves were discovered. From that time the fact took its place in science that the posterior roots

piquant ces racines, l'animal témoigne de la douleur ; mais elle n'est point à comparer pour l'intensité avec celle que se développe si l'on touche, même légèrement, la moelle épinière à l'endroit où naissent ces racines. Presque toutes les fois que l'on excite ainsi les racines postérieures il se produit des contractions dans les muscles où les nerfs se distribuent ; ces contractions sont cependant peu marquées, et infiniment plus faibles que si on touche la moelle elle-même. Quand on coupe à la fois un faisceau de racine postérieure, il se produit un mouvement de totalité dans le membre où le faisceau va se rendre.

" J'ai répété les mêmes tentatives sur les faisceaux antérieurs, et j'ai obtenu de résultats analogues, mais en sens inverse ; car les contractions excitées par le pincement, la piqûre, etc., sont très-fortes et même convulsives, tandis que les signes de sensibilité sont à peine visibles. Ces faits sont donc confirmatifs de ceux que j'ai annoncés ; seulement ils semblent établir que le sentiment n'est pas exclusivement dans les racines postérieures, non plus que le mouvement dans les antérieures. Cependant une difficulté pouvoit s'élever. Quand, dans les expériences que précèdent, les racines ont été coupées, elles étaient continues avec la moelle épinière : l'ébranlement communiqué à celle-ci ne serait-il pas la véritable origine soit des contractions, soit de la douleur qu'ont éprouvées les animaux ? Pour lever ce doute, j'ai refait les expériences après avoir séparé les racines de la moelle ; et je dois dire qu'excepté sur deux animaux, où j'ai vu des contractions quand je pinçais ou tirais les faisceaux antérieurs et postérieurs, dans tous les autres cas je n'ai observé aucun effet sensible de l'irritation des racines antérieures ou postérieures ainsi séparées de la moelle."—(*Ibid.*, p. 368.)

* " On voit par cette citation d'un ouvrage que je ne pouvois connaître, puisqu'il n'a point été publié, que M. Bell, conduit par ces ingénieuses idées sur la système nerveux, a été bien près de découvrir les fonctions des racines spinales ; toutefois le fait que les antérieures sont destinées au mouvement, tandis que les postérieures appartiennent plus particulièrement au sentiment, paraît lui avoir échappé : c'est donc à avoir établi ce fait d'une manière positive que je dois borner mes prétentions."—(*Ibid.*, p. 371.)

are for sensation and the anterior for motion. Some discussion has arisen as to whether the anterior roots do not possess a certain degree of sensibility, called recurrent sensibility, and this question has engaged the attention of physiologists with a few years; * but the distinct functions of the two roots have never been doubted. It has already been seen what use Bell made of these facts in late editions of his work on the nervous system. Before the days of anesthetics, exposing the roots of the nerves in the dog was very laborious, and painful to the animal, and the disturbances produced by so serious an operation interfered somewhat with the effects of irritation of the different roots. But now that the canal may be opened without pain to the animal, the experiments are much more satisfactory and have often been repeated by physiologists. I have frequently, indeed, demonstrated the properties of the roots of the nerves in public teaching.†

Although, as has been seen, almost all physiological writers, even in France, regarded Bell as the real discoverer, Magendie continued to claim that he first positively ascertained the seat of motion and sensation in the spinal nerves. In 1823, after reiterating his statements in regard to the nerves, he extended his researches to the cord itself, and demonstrated that the anterior columns are motor and the posterior columns sensory.‡ In all his subsequent publications the same statements are made.*

* Bernard, "Leçons sur la physiologie et la pathologie du système nerveux." Paris, 1858, tome i., p. 20, *et seq.* Even Bernard, a pupil, and for a long time the "préparateur" for Magendie, at one time seemed to regard Sir Charles Bell as the discoverer of the functions of the roots of the spinal nerves (*ibid.*, p. 25, and "Leçons sur les effets des substances toxiques et médicamenteuses." Paris, 1857, p. 20); in a late work, however, in which this whole subject is reviewed, the claims of Magendie to the discovery are fully recognized (Bernard, "Rapport sur les progrès et la marche de la physiologie générale en France." Paris, 1867, pp. 12 and 154). Bernard states that he was unable to obtain the original memoir of Bell, printed in 1811, but finally procured an exact copy, which is probably the reprint of 1839. (*Ibid.*, p. 155.)

† Flint, "Experiments on the Recurrent Sensibility of the Anterior Roots of the Spinal Nerves."—"New Orleans Medical Times," 1861, p. 21, *et seq.*

At the time that this paper was written, I had not had an opportunity of consulting the original memoir of Sir Charles Bell, and, with others, I regarded him as the discoverer of the functions of the roots of the nerves. I have also had occasion to modify the views therein expressed concerning the recurrent sensibility of the anterior roots.

‡ Magendie, "Note sur le siège du mouvement et du sentiment dans le moelle épinière."—"Journal de physiologie," Paris, 1823, tome iii., p. 153, *et seq.*

* Desmoulins et Magendie, "Anatomie des systèmes nerveux des animaux

Shaw, in his "Narrative," states that in 1822 Magendie "admitted that the experiments on the roots of the spinal nerves, which he had claimed as original, had been performed many years before by Sir Charles Bell." * This is not correct; and I have already quoted in full the passage in which Magendie gives Bell full credit for what he had done, but expressly states that the fact that the anterior roots preside over movements and the posterior over sensation seems to have escaped him. Shaw also quotes Desmoulins and Magendie as admitting "that there is no absolute distinction between the functions possessed by the two roots;" † but in doing this he translates the expression into English incorrectly. In the passage referred to, it is stated that "L'isolement des deux propriétés dans chacun des deux ordres de racines, n'est donc pas absolu," which simply means that the motor roots are not absolutely without sensibility and the sensory roots are not absolutely devoid of motor properties.

The experiments of Magendie made in 1822 must stand without further question as the first to demonstrate the true properties of the two roots of the spinal nerves; and before the publication of these experiments no physiologist had a correct idea, theoretical or experimental, of the seat of motion and sensation in these nerves. There can be no doubt that the honor of this discovery belongs exclusively to Magendie.

CONCLUSION

In its bearing on future knowledge in physiology, no discovery can be regarded as equal to that of the circulation of the blood, by Harvey. But since this, which marks a great epoch in science, there has been nothing so important as the location of the properties of motion and sensation in different portions of the cerebro-spinal nervous system. From this dates nearly all positive knowledge concerning the functions of this system. For many years the credit of this great discovery has been either indefinitely or incorrectly assigned by the great majority of physiological writers, simply because few had an opportunity of consulting for themselves the original pamphlet in which

à vertèbres." Paris, 1825, tome ii., p. 777. Magendie, "Précis élémentaire de physiologie," deuxième édition. Paris, 1825, tome i., pp. 167, 216, et quatrième édition, 1836, tome i., pp. 200, 266. * *Op. cit.*, p. 156. † *Op. cit.*, p. 168.

the first observations of Charles Bell, the reputed discoverer, are contained. If Bell or his defenders had published this memoir, which is only twenty pages in length, entire, he would undoubtedly have received full credit for all the advances which he really made in the physiology of the nervous system, and no injustice would have been done to others. Having obtained a complete and authentic reprint of the original memoir, I have endeavored to review it carefully and dispassionately, quoting all the passages which bear upon the functions of the nerves, in the hope of being able to settle forever the respective claims of Sir Charles Bell and Magendie to this discovery. From a review of this and other papers by Walker, Bell, Shaw and Magendie, the following conclusions are inevitable:

Like many great discoveries, the idea, and the experiments by which it was carried out and elaborated, did not emanate from a single mind.

In 1809, Alexander Walker proposed for the first time the theory that the properties of motion and sensation in the mixed nerves were derived from the two roots by which they take their origin from the spinal cord. This idea was entirely theoretical; and sensation was assigned to the anterior root and motion to the posterior root.

In 1811, Charles Bell, who was the first to experiment on the spinal nerves in animals recently killed, ascertained by experiment that the posterior roots of the spinal nerves had hardly any motor properties. He ascribed both motion and sensation to the anterior roots and supposed that the posterior roots presided over what are now known as the vegetative, or organic functions. He knew nothing about the sensibility of the posterior roots.

In 1822, F. Magendie, who was the first to experiment on the spinal nerves in living animals, ascertained by experiment that the anterior roots of the spinal nerves presided over movement and the posterior roots over sensation. He believed these to be distinct functions of these roots, but he thought at that time that the anterior roots might be slightly sensitive and the posterior roots might possess some motor properties.

From the experiments of Magendie dates all positive knowledge of the physiological properties of the two roots of the spinal nerves.

V

EXPERIMENTAL RESEARCHES ON POINTS CONNECTED WITH THE ACTION OF THE HEART AND WITH RESPIRATION

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1861.

It is not intended in this paper to take up all points connected with either of the functions which will come under consideration. This of course would be inconsistent with its scope; for many are so demonstrable and now so well established that their consideration here would be a mere recapitulation of facts well known and universally admitted. It is rather my object to present some original experiments by which I hope to elucidate points which are yet subjects of dispute among physiologists and which, in my opinion, cannot be settled by argument alone, but are capable of being brought under direct observation and if established can be made subjects of actual demonstration. Some functions can not as yet be disclosed to the senses in their natural operation; but others, which are connected with questions here to be considered, require only correct description to serve as facts from which each inquirer may make his own deductions. For the understanding of those processes which can easily be described and about which there can be no mistake, nothing usually is necessary but simple observation; but there are others, more delicate and obscure, which different experimenters see in different ways. In the investigations into their phenomena one should strive to perfect methods of observation, to devise means by which all confusing circumstances may be removed, to invent instruments which will make them more prominent, so that any observer, willing to take the trouble to look for himself, can see and interpret them in but one way. This is no less a

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desideratum in physiological than in pathological investigations; and means of physical exploration should be sought which will be to the physiologist what the stethoscope, the speculum, the ophthalmoscope and our many modern exploring instruments are to the pathologist. Obstetricians might differ in regard to conditions of the os uteri, exploring only by the touch, when the speculum, exposing the parts to the eye, would leave no room for discussion; auscultators, listening with the naked ear through the clothing of a patient, might dispute about sounds heard within the thorax, when they would agree if a stethoscope were applied to the naked chest. Thus, perfected apparatus enables the chemist and physiologist to demonstrate facts that would be obscure with less certain means of investigation. Many points in the physiology of the heart and of respiration are yet undecided; and it is by removing some sources of self-deception in the simple observation of phenomena and by multiplying demonstrable facts, the only true basis of general deductions, that I have endeavoured to go a step beyond what is already known and established.

The questions which I shall take up in this essay are, with reference to the heart:

First: Does the organ shorten or elongate during its ventricular systole, or contraction?

Second: How far is it possible to determine the cause of its regular and periodic action?

Third: What are some of the causes of arrest of the action of the heart?

Fourth: What is the mechanism of some of the nervous influences over the action of the heart?

Fifth: What is the mechanism of the action of the valves which guard the orifices of the heart?

And, in regard to respiration: What is the cause, and where is the seat of the impression, or "*besoin de respirer*," which is conveyed to the respiratory centre and which excites the action of the muscles of inspiration?

These questions have either never been fully understood by physiologists or are now explained in a contradictory manner in the various systematic physiological treatises.

It was with the hope of contributing something to the further elucidation of these obscure and disputed points that the experiments which form the basis of this paper have been undertaken.

CHANGES IN CONSISTENCE, POSITION AND FORM OF THE HEART DURING ITS ACTION.—In regard to the movements and action of the heart, there is manifestly but one correct mode of study, and that is the one which led Harvey to make the discovery of the circulation of the blood. This method is to expose the heart in living animals during its action and observe its movements. This may be done in various animals and in different ways. It is easy to observe the heart in action in the cold-blooded animals, by simply removing the anterior walls of the thorax; and its contractions will continue for a long time after such an operation and even after the organ has been entirely separated from the body. Such observations give a great deal of information but are made more valuable when compared with phenomena observed in warm-blooded animals, in which the heart resembles the corresponding organ in man. In operating upon the heart of these animals, such as dogs, cats, sheep or horses, it is necessary to keep up artificial respiration, as this function can not, of course, be performed by the animal after the thorax has been opened. Here it is convenient as well as humane to abolish sensibility by some means which will not interfere with the heart's action. This may be done by crushing the medulla oblongata in such a way as to avoid hemorrhage, as done by Erichsen and Pavy, of London; by stunning the animal with a blow upon the head, as done by Drs. Pennock and Moore; by decapitation and ligature of the vessels of the neck, as done by Legallois; by inoculation with curara or by the administration of ether or chloroform, which are the most convenient methods and those now most commonly employed by physiologists. The experiments which I have made have been performed upon animals rendered insensible by curara or ether; and I have been accustomed to operate in the following way:

The animal, preferably a good-sized dog, is first poisoned with curara by injecting about a grain of this substance into the subcutaneous areolar tissue or is completely

etherized. If poisoned with curara, its effects are watched, and in ten to thirty minutes the dog comes under its influence; more readily, if he is made to move about. If ether is used, he is rendered insensible in the ordinary way. The trachea is then opened and the nozzle of a bellows is introduced for the purpose of keeping up artificial respiration. An incision is then made in the median line from the top of the sternum to a point a little below the ensiform cartilage, through the skin, fascia and fat. The next step is to cut through the superficial muscles the whole length of the sternum on each side, about an inch from the median line, down to the costal cartilages, and then to tear away the muscles from the chest, exposing the ribs. The next step, after having exposed the chest in this manner, is to saw through the sternum in the median line, opening into the thoracic cavity; then to hold open the chest by sticks, or what is more convenient, to cut across the ribs on each side with a pair of strong cutting pliers, turn back the anterior walls of the thorax and retain them in that position by a strong ligature passed under the back of the animal and firmly tied. In this way, the lungs, which are regularly inflated with the bellows, are exposed and between them is seen the heart enclosed in its pericardium. The pericardium may then be removed by slitting it up and cutting it away from its attachments at the base of the heart, which may then be observed in the natural performance of its functions.

When the heart of a dog is exposed in this way, one of the most constant effects is an increase in the rapidity of its contractions. The pulse of a dog is always irregular in a state of health, varying between 100 and 120 beats in the minute. When the heart is exposed its pulsations become more frequent, sometimes numbering 200 to 250.

The phenomena which are observed in connection with the contraction of the ventricles are:

I. **HARDENING.**—This is a phenomenon constantly attending muscular contraction. It was described by Harvey, who proved that it took place during contraction of the ventricles, by introducing a small canula through the walls of the left ventricle, applying the hand to the heart and noticing that the hardening took place when a jet of blood was forced through the canula. Nearly all physio-

logical authors are agreed on this point, although Dr. Wood, late of the University of Pennsylvania, was of the opinion that the heart hardens during the diastole. I have repeatedly verified the fact that the heart hardens during the systole by repeating the experiment of Harvey. One who examines the heart in action can hardly be mistaken in regard to this point.

II. TILTING UPWARDS OF THE POINT OF THE HEART AND LOCOMOTION OF THE APEX FROM LEFT TO RIGHT.—About this phenomenon there is no difference of opinion. It can easily be observed in vivisections, and this movement would be expected from the spiral and oblique course of the superficial fibres of the heart from right to left, arising at the base and inserted, as it were, into the apex, which is free.

III. TWISTING FROM LEFT TO RIGHT.—This can be observed by examining the apex of the heart. It is universally admitted by physiologists and is explained by the spiral course of the fibres from right to left. This phenomenon, like the preceding, I have repeatedly observed.

IV. ELONGATION OF THE VENTRICLES.—This change in the length of the ventricles is denied by modern French, English and German physiologists, who seem all to agree that Harvey was wrong in this part of his description of the action of the heart. Harvey, Vesalius, Riolan, Fontana, Borelli, Winslow and Queye contended for the elongation of the organ during its systole; but this view was combated by Steno, Lancisi, Bassuel and Haller. It seems to me that the prevalence of the opinion, at the present day, that the heart shortens during systole can be attributed in great measure to the weight of the opinion of Haller. I am fortunate in having an opportunity of referring to an edition of his original works, published in 1757, and could not but be struck with its similarity in views, in arguments, and sometimes even in actual mode of expression, when treating of the change in the length of the heart during the systole, with the works on physiology which are now used as text-books, especially those by French authors.

Haller bases his views on his own experiments upon a case of ectropy of the heart ("Denique in puero, cui cor extra pectus propendebat, cor in diastole longius, et in sys-

tole brevius factum est, perinde ut in bestiis videmus" *) and on an argument of Bassuel. This last argument against the elongation of the heart is employed by many physiologists of the present day. Haller, after stating the views and arguments of Vesalius, Riolan and others, says:

"Varia nuperrimi scriptores reposuerunt. Et quidem Cl. Bassuel ad argumentum a valvulis venosis repetitum respondit, earum fabricam contra adversarios facere. Si enim in systole cordis mucro a basi recideret, tunc certe sequeretur, ut adtractis ad apicem funiculis, valvulae in cordis caveam deductae ostium aperirent, sanguinique venoso eam viam referarent, quam utique clausam esse oportet, dum cor contrahitur Mihi vero videtur, valvulas quidem venosas eo tempore a sanguine versus aures repulso extrorsum, inque aurium cavitates cessuras, nisi a musculis suis papillaribus, eo ipso tempore se decurtantibus, retinerentur, inque ventriculum reducerentur.

"Aliud experimentum addidit Cl. Bassuel; cor nempe aqua replevit, viditque, dum brevius fiebat, aquam expelli." †

I have exposed thus fully the views of Haller on this subject, because of the commanding influence he so long exercised in the physiological world, and especially because, on this point, late authors seem to have followed him so closely. In addition it may not be uninteresting to cite a few of the authorities who favor the shortening of the heart during its systole.

Todd, in the article on the heart in the "Cyclopedia of Anatomy and Physiology," speaking of the organ during its systole, says: "In all warm-blooded animals, at least, it becomes shortened."

Carpenter, in the "Principles of Human Physiology," London, 1855, page 226, says:

"During their contraction, the form of the ventricles undergoes a very marked change, the apex of the heart being drawn up towards its base, and its whole shape becoming much more globular."

Kirkes, "Handbook of Physiology," in speaking of the action of the ventricles, says:

"They contract much more slowly than the auricles, and simultaneously in every part, the whole wall of each ventricle being drawn up uniformly towards the origin of the artery at its base, diminishing the cavity in every diameter, but especially in length, so that the heart assumes a shorter and more globular form than it had in the relaxed and distended state of the ventricles."

* "Elementa Physiologiae," tome i., p. 392.

† *Ibid.*, tome i., p. 391.

Among the French authors is Bécлар, "Traité de physiologie," Paris, 1856:

"Le Raccourcissement général de l'organe, au moment de la contraction des oreillettes, est assez limité. Son plus grand raccourcissement coïncide avec la contraction des ventricles, qui l'emporte par dimensions les oreillettes" . . . "chez quelques animaux, le raccourcissement suivant la verticale est moins prononcé que le raccourcissement sur l'horizontale, ce qui a fait penser faussement à quelques observateurs que le cœur s'allonge pendant la systole ventriculaire."

Richerand, "Éléments de physiologie," tome i., p. 478, says:

"D'après cela, il est évident que le cœur se raccourcit," meaning during the systole.

Béraud, "Éléments de physiologie," revus par Ch. Robin, tome ii., p. 277, says, speaking of the systole:

"Le sommet des ventricles se rapproche de la base et du sommet, il suit de là que le cœur se raccourcit."

Magendie, "Précis élémentaire de physiologie," tome ii., p. 395, says:

"Les partisans de l'allongement ne persistent plus; mais il restait à démontrer comment, les ventricules se raccourcissant, le cœur se porte en avant."

Bérard, "Cours de physiologie," Paris, 1851, tome iii., p. 603, speaking of the systole, says:

"Le sommet des ventricules se rapproche de la base, et la base du sommet; il suit de là que le cœur se raccourcit."

M. H. Milne Edwards, in his "Leçons sur la physiologie et l'anatomie comparée de l'homme et des animaux," tome iv., p. 19, now in course of publication, in speaking of the systole of the heart, says:

"En effet, il devient presque circulaire à sa base; la portion voisine de la région ventriculaire se bombe d'une manière assez régulière, et la portion inférieure qui avoisine la pointe rétrécit et se raccourcit."

Finally, in the "Traité de physiologie considérée comme science d'observation," par C. F. Burdach, Professor à l'Université de Königsberg, translated into French by Jourdan, are to be found the opinions of the German physiologists; for Burdach was assisted in the preparation of this

work by Baer, Mayen, Meyer, J. Müller, Rathke, Valentin, and Wagner: tome vi., p. 234, he says:

"La contraction, ou systole, s'opère avec la rapidité de l'éclair. Le cœur se resserre sur lui-même; il devient plus ferme et plus dur; il se raccourcit, c'est à-dire que sa base et son sommet se recourbe un peu."

It is thus seen what a weight of authority there is in favor of the shortening of the heart during the systole, all of the English, French and German authors holding this opinion, and all of them denying the description of Harvey, who states that the heart elongates during contraction; "that it is everywhere contracted, but more especially towards the sides, so that it looks narrower, relatively longer, more drawn together." * It is only in this country that this opinion has been controverted; and though experiments have been made in England, with reference to this point,† they confirmed the prevalent view, and American experiments thus far have stood alone.

In November, 1839, Drs. Pennock and Moore made a number of experiments upon the hearts of rams and young calves, in order to settle disputed points in the change of the form of the heart during its action, and the mechanism of the production of the heart sounds. These were published in the "Philadelphia Medical Examiner," No. 44, and also in the American edition of "Hope on the Heart," 1846, page 59. It is not my object minutely to detail these experiments; I shall simply state that the animals operated on were stunned by a blow on the head, a bellows was introduced into the trachea, by means of which artificial respiration was kept up, the chest was opened and the movements of the heart were observed. With reference to the form and length of the heart during its systole, in all of these experiments, Drs. Pennock and Moore found that the heart elongated. Its elongation was measured with an ordinary shoemaker's rule and found in one experiment on a ewe one year old, to be one-quarter of an inch.

There are many sources of difficulty in examining a phenomenon apparently so simple as that of elongation

* Harvey's Works, published by the Sydenham Society, page 21.

† Experiments on the Motions and Sounds of the Heart, by the London Committee of the British Association for 1838-'39 and 1839-'40. Experiments for 1839-'40. "Hope on the Heart," Amer. ed., 1846, p. 65.

or shortening during the systole of the heart. In the first place, in the warm-blooded animals, as the dog, the heart's action is so rapid that it is difficult at first to determine, even, which is the systole and which is the diastole. Then in examining the heart, when the lungs are being alternately filled and emptied, partly covering the organ at each expansion, its apex only is seen, and it seems to retract when the heart contracts. In order to demonstrate the period of contraction in systole of the ventricles, I have employed the proceeding of Harvey, pushing a small silver tube through the walls of the heart into the left ventricle, withdrawing the stylet; and at each systole, a small jet of blood is forced through the tube, which enables one to determine at a glance when it takes place. In order to determine the period of elongation and shortening of the heart, I have devised an apparatus by means of which this phenomenon is exaggerated.*

In reasoning from the action of the heart in the lower animals to the corresponding movements in man, one should take into consideration the similarity in structure and arrangement of the organ and also take care that the ordinary conditions of life should approximate as nearly as possible to those in the human subject. For this reason, the most valuable experiments are on the warm-blooded animals; and the phenomena found here are not always verified in animals lower in the scale. I have not touched upon the change in form of the heart in the cold-blooded animals in the body of this paper; for although such investigations are interesting in themselves, they do not teach much in regard to human physiology. I may here state, however, that in the turtle the heart shortens during systole. This is due to the thinness of the ventricle and the great size of its cavity compared with the warm-blooded animals. The heart of the frog, also, shortens slightly during systole, and I have been able to measure the actual extent of shortening with a pair of ordinary dividers. An American observer † has described an experiment, which

* Since the publication of this article in 1861, I have become convinced, by a number of more exact observations on the exposed heart, that the ventricles shorten during their systole. I have therefore omitted the wood-cut and description of the apparatus which I devised and which seemed to show elongation of the ventricles.

† Dalton's "Treatise on Human Physiology," 2d edition, p. 258.

I have often repeated, to prove the elongation of the frog's heart during contraction, which consists in holding the heart by the base between the thumb and finger, with the apex upward, and irritating it with the point of a needle. At each irritation the apex is elevated, giving an appearance of elongation. This appearance is not deceptive; the heart actually elongates, but the position in which it is held, the ventricle being empty, causes its flaccid walls during relaxation to collapse, shortening the heart more than is natural. The same experiment I have repeated with the heart of the turtle; but in altering the position of the heart and allowing the apex to hang downward, the heart will be found to shorten during the systole, the dependent apex being drawn up by the muscular contraction. These experiments prove nothing one way or the other. It is better, in all experiments of this description, to observe the heart in situ, while its cavities are filled with blood. In observations upon the irritability and various properties of the anatomical elements of the heart, phenomena in cold-blooded animals may be studied with advantage; for here the properties are the same, modified only by the vital condition of the animal, which, by diminishing the intensity of their manifestations, render their study more simple.

The following experiments were made in regard to the change in the length of the heart during the systole or contraction:

EXPERIMENT I. January 28, 1861.—A good-sized dog was poisoned with curara, artificial respiration was kept up, and the heart, which was beating strongly and naturally, was exposed in the usual way. Upon holding the base of the heart between the index and middle fingers, the thumb, placed upon the apex, was sensibly raised at each systole, which was marked by the hardening of the ventricles. The mekeoscope* was now applied and indicated elongation with every systole, or contraction of the ventricles. The systole of the heart was also marked by slight corrugation of the surface of the ventricles, by a tilting movement of the apex upwards and from left to right and by a twisting movement of the heart on its axis, from left to right.

EXPERIMENT II. February 1, 1861.—A medium-sized dog was etherized and the heart exposed in the usual way. The facts which are recorded in Experiment I were demonstrated upon this animal. The mekeoscope was applied to the heart, which was acting nor-

* The instrument designed to show elongation of the ventricles, the description of which has been omitted.

mally, and indicated elongation during the systole. This point was verified by several medical gentlemen. The upper extremity of the indicator moved one-half an inch to an inch with every beat of the heart. It was determined that the heart elongated during the systole, by introducing a small silver canula into the left ventricle and noticing that the indicator showed elongation every time a jet of blood was forced through the canula.

EXPERIMENT III. February 8, 1861.—A large dog was poisoned with curara and the heart exposed in the usual way. The heart was pulsating well; the mekeoscope was applied, and elongation during the systole was demonstrated. The various points recorded in Experiment I were confirmed in this animal.

EXPERIMENT IV. February 15, 1861.—A medium-sized dog was etherized and the heart exposed in the usual way. The mekeoscope was applied and the points recorded in the preceding experiments were confirmed.

EXPERIMENT V. February 19, 1861.—A good-sized dog was etherized and heart exposed in the usual way. The points recorded in the preceding experiments were confirmed in this.

CONCLUSIONS.—From the five observations here reported, which I have repeatedly confirmed in unrecorded experiments, there is one legitimate conclusion; viz., that the heart of the dog elongates during the systole, or contraction of the ventricles. In reasoning from the inferior animals to the human subject, taking into consideration the anatomical characters, it is found that the heart in the dog has essentially the same anatomy as in man; but instances are on record where the heart has been exposed to observation in the human subject. Harvey states, in his report of the remarkable case of the son of the Viscount Montgomery:

“We also particularly observed the movements of the heart, viz., that in the diastole it was retracted and withdrawn, while in the systole it emerged and protruded; and the systole of the heart took place at the moment the diastolic impulse in the wrist was perceived: to conclude, the heart struck the walls of the chest, and became prominent at the time it bounded upwards and underwent contraction of itself.” *

Haller states that in the case of *ectopia cordis* which he had an opportunity of observing, the heart shortened during its systole, as it did in animals that he examined. Both of these physiologists had the opportunity of examining the action of the heart in the human subject, and both verified their previous observations on animals, although the results were contradictory.

* Harvey's Works, published by the Sydenham Society, page 384.

It seems, then, a legitimate conclusion that in man, as in the animals examined, the heart elongates during its systole.

Having come to this conclusion from actual observation, the next step is to endeavour to account for it by the anatomical arrangement of the muscular fibres of the heart. This can easily be done; for if a heart is boiled so as to dissolve the areolar tissue which holds together its muscular bundles, the fibres can easily be separated and traced. On the outside is a layer of fibres, common to both ventricles, taking a spiral course from left to right, from the base to the apex. Removing these superficial fibres, beneath them is found a mass of circular fibres, enveloping separately the right and left ventricles. The action of these circular fibres in shortening is, of course, to increase in diameter; and this increase in diameter, from the arrangement of the fibres, would produce elongation of the body of the heart.

The powerful action of these deep circular fibres of the heart is also shown by a phenomenon noticed during contraction; namely, the production of rugæ on the surface of the ventricles. This appearance is not mentioned by Harvey but is noticed by Haller in the work I have before quoted, vol. i., page 389.

"Quando cor quietum, aut relaxatum, a stimulo quocunque in motum cietur, tunc apparent in externa cullis superficiæ rugæ, in quas fibræ contractæ crispantur, undulatæ, in rana et anguilla evidenter transversæ, neque in cane, fele, aut aliis calidi sanguinis animalibus obscuræ."

This may be because the superficial fibres, being exposed to the air, are more irregularly and less powerfully contracted than the deep, or it may be a phenomenon which always takes place. At all events, it indicates that the powerful contraction of the deep circular fibres throws the superficial fibres into slight longitudinal folds from the greater efficiency of their action; and that the superficial fibres, which from their arrangement might tend to shorten the heart, do not compress, in their contraction, the deep fibres, but that the latter are the more powerful agents in the systole. Thus what is demonstrated by observation of the action of the heart in the living animal may easily be accounted for by the anatomical arrangement of its muscular fibres.

In regard to the hypothesis of Bassuel, which is so often quoted, that elongation of the heart, by putting the chordæ tendineæ on the stretch, would prevent the closure of the auriculo-ventricular valves and therefore is impossible, I have nothing to say. It seems to me sufficient to have demonstrated on the living animal the elongation; and I have this simple fact to oppose to any hypothetical objection.

CAUSE OF THE RHYTHMICAL CONTRACTIONS OF THE HEART.—The cause of the regular and intermittent contractions of the heart is obscure; and the experiments that I have made on this subject, though far from being so satisfactory as the preceding, still, I conceive, define the extent of actual knowledge and bring to light some laws which regulate the action of this organ. It was first supposed that the blood circulating through the heart was the cause of its rhythmical contractions; but the heart will continue to beat regularly after it has been emptied of blood and has been removed, indeed, from the body. The atmosphere was then supposed to supply the place of the blood as a stimulus; but the heart of a frog has been placed under the receiver of an air-pump and still it continued to pulsate. Without going farther into the opinions now entertained by physiological writers, it is sufficient to state that physiologists are not yet fully acquainted with the real cause of the rhythmical contractions of the heart; and the following experiments were made in the hope of throwing some light upon this obscure subject.

EXPERIMENT VI.* November 14, 1860.—An alligator, six feet in length, was poisoned with curara, the thoracic cavity opened and the heart exposed. Some experiments were then made upon this organ which will be detailed in another place; but, twenty-four hours after the operation, the heart, which had been left in situ, was found beating regularly and with considerable force.

EXPERIMENT VII. January 28, 1861.—An alligator of the same size as the one used in Experiment VI. was poisoned with curara, the chest opened and observations made upon the heart. The heart was left in situ and twenty-four hours after death was found pulsating vigorously and regularly. The auricles were then stimulated with an ordinary magneto-electric apparatus during the intervals between the movements of the organ; they immediately contracted, and their contraction was immediately followed by contraction of

* For the anatomy of the heart of the alligator, see Appendix.

the ventricles. Upon applying the stimulus to the ventricles they contracted, contraction of the auricles following immediately. These phenomena were repeatedly verified in the presence of two assistants; the same results followed irritation with the point of a scalpel. The heart was then removed from the body and emptied of blood. When placed upon the table it pulsated quite rapidly (about ten times per minute instead of four or five) but its contractions were feeble. On stimulating the ventricles, they contracted powerfully, feeble contractions of the auricles following. On stimulating the auricles, they generally contracted feebly and sometimes no movement was excited; but the ventricles contracted invariably.

The aortæ (there are two in the alligator) were then tied and the heart was filled with blood (which was prevented from coagulating by the addition of a little solution of carbonate of soda) by injecting it through the right auricle and confining it with a ligature. The heart then began to contract regularly and forcibly. The auricles contracted first, and then the ventricles, making about four pulsations per minute. The contractions were powerful and regular, contrasting strongly with the rapid and feeble action before the organ had been filled with blood. The heart was evidently over-distended, but was relieved by dividing the coronary artery, allowing some of the blood to escape, until it was reduced to about its normal condition of fullness. Electric stimulation of the auricles excited contraction, followed by contraction of the ventricles, and the same stimulus applied to the ventricles excited contraction, followed by contraction of the auricles, in about the same manner as when these experiments were made upon the organ before its removal from the body. This, also, was repeatedly verified. The heart was then emptied of blood and placed upon a clean plate. The contractions became such as were noted immediately after the heart had been removed from the animal and before it had been filled artificially with blood.

The heart was then filled with water. The contractions were not so powerful and regular as when it had been filled with blood, and were limited chiefly to the ventricles. They were also much more rapid. It was impossible to establish the contraction of the auricles on electric stimulation, followed immediately by contraction of the ventricles, and the reverse, as when the heart was filled with blood. The ventricles, still filled with water confined in their cavity, were then firmly grasped in the hand so as to subject the muscular fibres to powerful compression. From that time the heart entirely ceased its contractions and became hard, like a muscle in a state of cadaveric rigidity. The experiment was then terminated twenty-eight hours after the death of the animal; and the heart was still beating until its pulsations were arrested in the manner described.*

EXPERIMENT VIII. On Turtles.—The hearts of turtles were

* These observations were begun twenty-four hours after the death of the animal.

exposed and removed from the body while pulsating. Electric stimulation applied to the auricles produced contraction, followed by contraction of the ventricle; and a stimulus applied to the ventricle produced a contraction, followed by contraction of the auricles. This took place whether the irritation was electric or mechanical, like the point of a needle, and indifferently whether the heart was removed from the animal or left in situ.

These observations were repeatedly verified upon the same turtles and in a number of subsequent experiments.

EXPERIMENT IX. March 11, 1861.—The heart of a turtle was removed and the ventricles separated from the auricles. The auricles contracted spontaneously and regularly for twenty minutes, the time during which their movements were observed; and the ventricle contracted irregularly and at intervals of two minutes or more. The ventricle always contracted when irritated with the point of a needle.

In this experiment I was not certain that the ventricle contracted without the application of a stimulus, for it was exposed to currents of air, jars of the table, etc., which might be capable of producing contractions.

EXPERIMENT X. March 13, 1861.—The heart of a turtle was removed from the body while it was beating regularly, and the ventricle was separated from the auricles as in the preceding experiment. Both auricles and ventricle were then placed under a bell glass and carefully observed for an hour and thirty minutes.

When placed under the bell glass, the auricles contracted regularly twelve to sixteen times per minute. No contraction of the ventricle occurred.

Five minutes after.—Auricles the same and the ventricle contracted once.

Seven minutes after.—Auricles contracting regularly sixteen per minute, ventricle contracted. (The apparatus was shifted from one table to another, which might have been the cause of the ventricular contraction.)

Ten minutes.—Auricles the same and ventricle contracted.

Eleven minutes.—Ventricle contracted.

Twelve minutes.—Ventricle contracting regularly five times in two minutes.

Twenty-two minutes.—Ventricle contracting regularly seven times in two minutes; auricles contracting twenty-two times per minute.

Thirty-two minutes.—Ventricle contracting four times per minute; contractions of auricles rapid but irregular.

Forty-two minutes.—One and three-quarter minutes between the contractions of the ventricle.

One hour and thirty minutes.—Auricles contracting eight times per minute; two minutes between the contractions of the ventricle.

EXPERIMENT XI. March 13, 1861.—The heart of a turtle was removed and placed under a bell glass.

Thirty minutes after.—It pulsated twelve times per minute, contraction of the auricles always preceding that of the ventricle.

Sixty minutes.—The heart pulsated six times per minute, the auricles contracting first.

In making these experiments, it was found that the operation of removing and dividing the heart produced a shock which interfered at first with its action. The heart recovered from it, however, in about thirty minutes.

EXPERIMENT XII. February 15, 1861.—A medium-sized dog was etherized and his heart exposed in the usual way, artificial respiration being kept up. While respiration was being actively performed by means of bellows and while the heart was pulsating vigorously, the organ was suddenly removed from the body by a single sweep of the knife. It was immediately placed upon the table and contracted so vigorously that it bounded up at every pulsation like an India-rubber ball. This remarkable phenomenon lasted for a few seconds only, but the heart pulsated regularly for two minutes. A powerful shock was then passed through it by means of a magneto-electric apparatus, with the effect of immediately arresting all regular pulsations; but this was followed by a general, irregular vermicular action of the fibres. This continued for thirty minutes. At first irregular contractions could be excited by feeble currents; but after thirty minutes this became impossible. When the vermicular action of the muscular fibres had ceased no contraction could be excited by electric or mechanical stimulus.

EXPERIMENT XIII. March 13, 1861.—A turtle was poisoned with a variety of curara which arrests or depresses the action of the heart, by injecting about a grain of it in solution under the skin. In thirty minutes the animal was dead and the exposed heart was found beating feebly and slowly. On applying electricity to the exposed muscles, their irritability was found, by actual comparison with the exposed muscles of turtles which had not been poisoned, to be very much diminished.

EXPERIMENT XIV. March 13, 1861.—The preceding experiment was repeated upon another turtle. When all signs of life had disappeared, the heart was exposed and found beating feebly. Muscular irritability was much diminished.

It will be seen by these few experiments that it is difficult, if not impossible, in the present state of knowledge and with such data alone, to say why the heart contracts in the manner which is characteristic of it. If the cause resides in the nervous system, it must be in nerve-centres existing in the substance of the organ. In short, the contraction of the heart is dependent either upon nerves in its substance or upon an inherent property peculiar to its muscular fibres. The nervous influence, if there is any, must come from the sympathetic or organic system, because an organ must remain connected with the cerebro-spinal centres in order that any influence should be derived from this system.

Dr. Robert Lee, of London, has demonstrated the existence of sympathetic ganglia in the substance of the heart; but it is impossible to say positively that an influence derived from these is the cause of its rhythmical contractions. The most that can be said on this subject is that the muscular fibres of the heart have an inherent property of contraction so long as they are in a state of physical and chemical integrity; that this contraction, like that of all other muscles, is followed by a relaxation; but the fibres of the heart, after the short period of repose which is thus allowed them, contract again. I know that in this statement I am simply describing the phenomena of the heart's action and confessing ignorance as to its cause; but we are in the best position to acquire information upon any subject when admitting the real state of knowledge, and not attempting to explain what, with our resources, is incapable of explanation.

I have given the sum of actual knowledge of the cause of the heart's action as an introduction to a study of some of the properties of the muscular fibres of this organ and the laws by which their contractions are regulated.

I. The muscular fibres of the heart possess in a remarkable degree that property known as irritability. This is more marked in the auricles than in the ventricles. The auricles contract readily upon the application of a stimulus applied to the surface; and Virchow has demonstrated that the internal surface is much more irritable than the exterior.

II. It has been shown by experiments made by Erichsen * that the action of the heart is arrested in about thirty minutes, in the warm-blooded animals, by ligature of the coronary arteries, artificial respiration being continued, showing that the presence of a certain quantity of blood in the substance of the organ is necessary to the irritability of its muscular fibres.

III. Experiments here detailed, as well as those of other

* These experiments were made by pithing the animal, keeping up artificial respiration and opening the chest. It was found that the heart continued to beat under these conditions, for one to two hours, but was arrested in a short time if the coronary arteries were ligated. The mean of six experiments showed the duration of the heart's action, after ligation of these vessels, to be 23½ minutes. The experiments are to be found in the "Medical Gazette," July 8, 1842.

observers, show that the heart of cold-blooded animals, especially the alligator, retains its irritability for a long time after death. In Experiment VII. the heart was beating twenty-eight hours after death, when its action was artificially arrested. This was due in part to the action of curara; for Bernard has lately shown that muscular irritability remains in frogs poisoned with this agent much longer than ordinary, and that the action of the heart is also prolonged.* This property renders curara valuable in studying the movements of the heart.

IV. The same experiments (on turtles and alligators) show that a stimulus, mechanical or electric, applied to one part of the heart is propagated to the other, and also tend to show that the stimulus which, in the natural action of the organ, excites the auricles to contraction, is propagated from them to the ventricles. These experiments are not new. The same fact has been noticed by Mr. Paget in the heart of the turtle and was published in the "British and Foreign Medico-Chirurgical Review," vol. xxi., p. 550.

V. Experiments IX. and X. show that the irritability of the auricles and ventricles are separate and distinct; that the auricles possess this irritability in a much greater degree than the ventricles, as demonstrated by the distinct contractions of auricles and ventricles when separated from each other and the much greater frequency of contractions of the auricles; that the contraction of the auricles acts as a stimulus to the ventricles, for when they are left together, as in Experiment XI., and the heart is removed from the body, the auricles always contract first, and their contraction is invariably followed by contraction of the ventricles.

VI. Experiment VII. shows that the heart of the alligator, if emptied of blood, does not contract regularly; but that its regular contractions return if the blood is injected into and confined in its cavities; also that the propagation of a stimulus from auricles to ventricles is not invariable in the heart emptied of blood, but that it may always be demonstrated in the heart filled with blood either naturally or artificially.

VII. The same experiment shows that the heart filled

* Bernard, "Substances toxiques et médicamenteuses," page 320 *et seq.*

with water does not act normally after removal from the body, as it does if blood is injected into its cavities, but more rapidly and less efficiently; and finally, that powerful compression seems to paralyze the muscular fibres instantly and cause them to take on cadaveric rigidity.

VIII. Experiment XII. shows that a powerful electric shock passed through the substance of the heart, in warm-blooded animals, immediately arrests its regular pulsations.

IX. Agents which abolish or diminish general muscular irritability, like the sulphocyanide of potassium, have a corresponding effect upon the heart. This is a fact now well established.

Experiments XIII. and XIV. show that a certain kind of curara, which arrests the action of the heart, diminishes very much the general muscular irritability.

CONCLUSIONS.—From the facts stated above, the following deductions can legitimately be made:

The natural stimulus of the regular movements of the heart is the blood; and this stimulus can not be adequately supplied by any other fluid of less density, like water; so that, in conditions in which the blood becomes watery, as in the reaction after copious bleeding or in anæmia, the contractions of the heart are feeble and rapid; and in affections in which the blood becomes denser than in health, as in plethora, the heart contracts more slowly and with abnormal force.

In the normal action of the heart, this stimulus first affects the auricles, which are first distended with blood, and is propagated thence to the ventricles.

All irritability of the muscular fibres of the heart may be immediately arrested by forcible compression; and its property of regular contraction may be abolished by a powerful electric current.

A peculiarity of the muscular irritability of the heart is that when the organ has ceased to contract spontaneously while in the chest or after removal from the body, contractions can not be excited by ordinary stimuli, such as irritation with the point of a needle or scalpel or electricity; while such irritation applied to any of the muscles will produce contractions. In an experiment which I made on

this point upon the heart of a dog, I found that the heart ceased beating in about ten minutes after the stoppage of respiration (the dog had been etherized and his heart exposed), and that after that time electric stimulation applied to the heart failed to produce contraction, although the sterno-mastoid and muscles of the chest, which had been exposed during the operation, contracted powerfully on the application of the stimulus. This favors the idea that the muscles of the heart differ from the other striped muscles in possessing the inherent property of regular contraction; for they continue to contract till they have lost their irritability, and then can not be excited to action artificially. This is true only when the heart is allowed to stop spontaneously and the duration of its pulsations is not interfered with by placing it in a vacuum (which, while it does not arrest, abridges the duration of the heart's action) or by other means.*

The irritability, which in ordinary muscles is manifested by their contraction upon the application of a stimulus, and, in the case of the heart, by regular pulsations so long as the fibres retain their integrity, is really identical in the heart and general muscular system; it is greatest in the heart and is much greater in the auricles than in the ventricles, as shown by experiments. In the heart this irritability becomes extinct before general muscular irritability is lost, for the regular contractions of the organ after death or after removal from the body wear it out, while the general muscular system, if unstimulated, is in a state of repose. It is also true that muscular, like nervous irritability, disappears soonest in parts where it is most intense, as it does in animals like the warm-blooded, the functions of which are most active. The ventricles seem to depend for their stimulus upon the contraction of the auricles; for when separated, as in Experiment X., the ventricles do not contract so frequently as the auricles, or so frequently as when their connection with them is not severed. The ven-

* I have not made a sufficient number of experiments to be able to state this positively, but it is certain that the general muscular irritability continues long after the heart has ceased to beat; and the question arises, in studying the heart of a cold-blooded animal in a quiescent state, but contracting upon irritation, whether it does not contract spontaneously but at remote intervals, as in Experiment X. This question can be answered only by more extended observations.

tricles possess, then, an independent irritability which is much less than that of the auricles.

The irritability of the heart is like the general muscular irritability in another respect. Most agents which paralyze the muscular system paralyze the heart; and Experiments XIII. and XIV. show that the peculiar variety of curara, which acts upon the heart, diminishes to a great extent the irritability of the general muscular system. On the contrary, the most common variety of curara, which paralyzes the motor nerves and the sympathetic system, leaves the muscular irritability intact, and also the movements of the heart, which will continue for a long time after death, if respiration is artificially performed.

MECHANICAL CAUSES WHICH ARREST THE HEART'S ACTION.—In asphyxia and in some organic diseases of the heart, there is arrest of the action of this organ. When this is caused by mechanical obstruction, as in disease at the aortic orifice, death is attributed to overdistension of the heart; but in asphyxia it becomes a question whether death is due to this cause or to the circulation of venous blood in its substance, as was supposed by Bichat. In experiments on the lower animals, when we expose the heart and keep up artificial respiration, we can easily see the immediate effects of arrest of respiration upon its action. It becomes distended, changes from a red to a blue color, showing that venous blood is circulating in its substance, and gradually its movements cease. But if respiration is recommenced before its action has been entirely arrested, it immediately becomes florid, its distension is gradually relieved and soon its normal action is reëstablished. In order to determine the cause of stoppage of the heart in asphyxia, I made the following experiments.

EXPERIMENT XV. February 1, 1861.—A dog was etherized at 2.15 P. M. and the chest opened in the usual way. At 2.25 I stopped respiration. In fifty seconds the heart became dark and much distended. Respiration was recommenced, which had the effect of soon restoring normal action. The pulmonary artery and aorta were then tied suddenly with a strong cord. The heart became much distended, was of a red color, labored more than when respiration had been stopped, and in forty seconds it became necessary to remove the ligature for fear of permanently arresting its action. After removing the ligature, the heart gradually returned

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to its normal condition, but more slowly than when respiration had been arrested for fifty seconds.

At 2.40 a grain of curara was injected into the areolar tissue. At 4.10 the aorta was compressed. The heart labored, and in twenty-five seconds the compression was removed and it gradually resumed its normal action. Respiration was then suspended with the same effect on the heart. In one minute respiration was recommenced and the heart resumed its normal action.

In this experiment compression of the aorta and pulmonary artery produced more trouble in the heart's action, the trouble came on more rapidly, and it was longer before its action became normal than when respiration was stopped; though when the vessels were compressed the heart was florid, showing red blood circulating in its substance, and when respiration was arrested it became dark.

EXPERIMENT XVI. February 8, 1861.—A large dog was poisoned with curara and the chest opened in the usual way. Respiration was stopped for two and a half minutes. The heart became very dark, much distended, and labored; but when respiration was recommenced it became gradually relieved, and in a few minutes regained its normal action. The aorta was then tied for two minutes. The heart remained red, became more distended, and labored more than in the previous instance, but gradually resumed its action after the ligature was removed. During the time that the aorta was compressed, here, as in Experiment XV, respiration was continued.

In this experiment I tried to ascertain how long the heart could be kept distended by asphyxia or compression of the great vessels and yet resume its functions when the cause of the distension was removed.

CONCLUSIONS.—Great distension of the heart will produce paralysis of its muscular fibres; and this is the cause of the arrest of its action in asphyxia and in many cases of sudden death, not the circulation of venous blood in its substance, as was supposed by Bichat. The experiments which I have detailed demonstrate this fact in regard to asphyxia; for here it is shown that the greater the distension the sooner the heart ceases its contractions. The heart is arrested sooner by ligature of the great vessels, when red blood circulates in its substance, than by arrest of respiration, when it is supplied with black blood, because in the first instance the distension is greater.

The mechanism of this muscular paralysis is the same

as that of the paralysis of any striped muscle by straining. If a muscle is violently extended, as in a dislocation, there is loss of function for a period proportionate to the severity of the strain. The same is true in regard to the heart; but the constant action of the heart is necessary to existence; and when this muscle is paralyzed by straining of its fibres by distension, the animal dies before it has time to recover its functions. In case of asphyxia, then, so long as the heart continues to act, though feebly and at long intervals, artificial respiration will probably restore life; but after its action has been suspended there can be little or no hope of restoring it.

Cases of sudden death from organic disease of the heart, contrary to the popular impression, are not common; and the only form of this affection in which sudden death is likely to occur is disease at the aortic orifice. In this form of the affection, the heart is liable to overdistension from any cause which increases the force and rapidity of its action; and death results from stoppage of the heart, in the same manner as when the aorta has been tied, as was done in the experiments before detailed.

In death from injury to the head, as from apoplexy, respiration is interfered with and distension of the heart occurs in precisely the same way as when artificial respiration is interrupted in experiments on the lower animals. This is further illustrated by the experiments of observers who stun the animals upon which they operate in order to observe the action of the heart. If artificial respiration is not immediately established, the heart ceases to act, from distension, and the animal dies.

In death from poisoning by opium, the respiratory muscles are paralyzed by the poison, and the heart ceases to act in the same manner as in asphyxia from any cause. It would then follow that if artificial respiration is kept up until the power of the poison is exhausted and natural respiration is gradually restored, the life of the patient would be preserved; and the well-known experiments of Sir Benjamin Brodie with opium and curara have proved that this is the fact.

In some cases of convulsions, when death occurs respiration is interfered with and the heart is arrested by overdistension. This is true of all nervous diseases which, from

their action upon the general system or upon the respiratory apparatus, produce death.

In death from introduction of air into the veins, the air going to the right side of the heart is divided into minute bubbles which can not pass through the lungs. The heart becomes distended from this obstruction and ceases to contract from overdistension.

It appears, therefore, that distension of the heart, by its mechanical action on the muscular fibres, may cause stoppage of the circulation and death; that sudden death may generally be attributed to this cause; that the cause of this distension may usually be referred to the respiratory function; and that the indications are, therefore, to reëstablish this function, by artificial respiration or otherwise, when it is arrested, or to prevent the diseases under which the patient may labor from interfering with it.

INFLUENCE OF THE PNEUMOGASTRIC NERVE ON THE ACTION OF THE HEART.—The heart, like other of the striped muscles, is provided with nerves derived from the cerebro-spinal system; but the action of the nerves which go to the heart differs from the nervous influence exerted upon any other muscle. If a nerve distributed to a voluntary muscle is divided the muscle is paralyzed; but after division of the pneumogastric nerve, which is distributed in part to the heart, this organ, far from being paralyzed, is accelerated in its action. Bernard has found that division of the pneumogastriks in the neck increases the number of cardiac pulsations, sometimes even doubling them; but that the force of the contractions is diminished. When the peripheral end of a divided nerve going to a muscle is faradized the muscle is thrown into violent contractions; but stimulation of the peripheral ends of the pneumogastriks arrests the action of the heart. These observations were made in 1845, by Weber, and have been repeatedly verified by physiologists since that time; but the cause of this peculiarity of action has not been satisfactorily explained.

In the first place it is important to determine whether the electric stimulus is conveyed to the heart directly through the motor filaments of the pneumogastriks or through the sensory filaments to the nerve-centres, and

by reflex action operates through other nerves on the heart. This is easily ascertained by dividing both pneumogastrics and stimulating alternately the central and peripheral ends; when it is found that the current applied to the peripheral extremities will arrest the action of the heart, while the same stimulus applied to the central ends produces no such effect. By means of curara, the motor nerves and the motor filaments of the mixed nerves are paralyzed, the two systems being dissected out, as it were, by this curious poison; and it is found that when the pneumogastric nerves are stimulated in an animal poisoned by this agent, it is impossible to arrest the action of the heart. This fact was pointed out by Bernard * and has been repeatedly verified by myself.

If both pneumogastric nerves of a dog are isolated in the middle of the neck and subjected to a feeble current, the first effect upon the movements of the heart, when this organ is exposed to view, is a diminution in the frequency of its pulsations. If the current is then gradually increased in intensity, the action of the heart is arrested; the heart remains dilated instead of contracted, and it ceases to act so long as the current is continued. When the current ceases the heart soon begins to beat and in a few minutes will have resumed its normal movements. This effect is produced in most of the inferior animals and can readily be shown in the frog, turtle, alligator and other cold-blooded animals, which are well adapted to experiments on the heart and on the nerves; but in birds, Bernard has not been able to demonstrate it; † for what reason, he does not state. When the current is applied directly to the heart, as I have done in some instances after the organ has been removed from the chest, if the current is sufficiently powerful, all regular pulsations cease and there is nothing but the irregular vermicular action which is observed when the irritability of this organ has become nearly exhausted. This fact I have observed in the heart of the dog.

Endeavoring to throw some light upon the cause of arrest of the heart's action by stimulation of the pneumogastrics, I made the following experiments upon the dog, turtle and alligator:

* Bernard, "Substances toxiques et médicamenteuses," p. 348.

† Bernard, "Physiologie et pathologie du système nerveux," tome ii., p. 394.

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EXPERIMENT XVII.—The heart of a large dog was exposed in the usual way while the animal was under the influence of ether. After the chest had been opened and while artificial respiration was being kept up, the pneumogastric nerves were isolated in the neck and a feeble current was passed through them with the magneto-electric machine used in former experiments.

The heart was arrested by quite a feeble current, in the manner above described. This was repeated several times. The action of the heart began again when the current was arrested.

EXPERIMENT XVIII.—The heart of a turtle was exposed and found contracting regularly. The pneumogastric nerves were then isolated in the neck and a feeble galvanic current passed through them. This was done by bending the ends of the conducting wires in the form of hooks and catching up each nerve. The action of the heart was immediately arrested. It began again when the current was interrupted and stopped when it was resumed.

EXPERIMENT XIX. March 13, 1861.—In a medium-sized dog under the influence of ether the carotids and pneumogastric nerves were exposed. The cardiometer was applied to the right carotid and the following observations were made:

Arterial pressure (constant).....	(Minimum) 125 millimetres.
At each action of heart.....	(Maximum) 130 "
Pulsations.....	5 "

The pneumogastrics were then divided. The movements of the heart became more rapid and the instrument marked:

Arterial pressure (very variable).....	100 to 150 millimetres.
Oscillations with heart's action.....	2½ "

The peripheral extremities were feebly stimulated. The action of the heart became slower and the instrument marked:

Minimum.....	40 millimetres.
Maximum.....	65 "
Pulsations.....	25 "

The current was then stopped and the instrument marked:

Minimum.....	147½ millimetres.
Maximum.....	150 "
Pulsations.....	2½ "

EXPERIMENT XX. March 11, 1861.—The pneumogastrics and carotids were exposed in a large dog in which the chest had been previously opened and the heart exposed while the animal was under the influence of ether. The cardiometer was applied to the right carotid and marked:

Minimum.....	40 to 45 millimetres.*
Maximum.....	40 to 50 "
Pulsations.....	5 "

* When the chest is opened the pulsations become more frequent and the pressure of blood is much diminished, as is seen by comparing these tables with those in the preceding experiment.

The pneumogastrics were then feebly stimulated. The pulsations of the heart were diminished in frequency and the instrument marked:

Pulsations..... 20 to 30 millimetres.

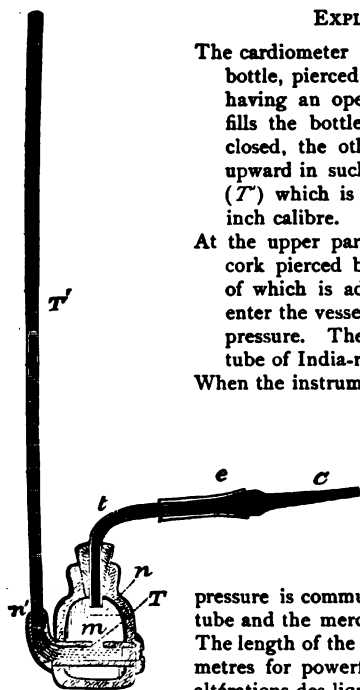
Experiments XVII. and XVIII. demonstrate the arrest of the heart's action by stimulation of the pneumogastrics in the dog and turtle. This fact is now established, and the two experiments here recorded are introduced merely to confirm previous observations.

EXPLANATION OF ILLUSTRATION

The cardiometer is composed of a thick and strong glass bottle, pierced by an iron tube securely soldered, and having an opening (*T*) by which the mercury which fills the bottle enters. One end of the iron tube is closed, the other projects from the bottle and bends upward in such a way as to receive at (*n'*) a glass tube (*T'*) which is graduated and which is $\frac{1}{4}$ to $\frac{1}{2}$ of an inch calibre.

At the upper part the bottle is hermetically sealed by a cork pierced by a tube (*t*) of glass or iron, at the end of which is adjusted a metallic tube (*C*) designed to enter the vessel in which it is desired to measure the pressure. The tube (*C*) is joined to the tube (*t*) by a tube of India-rubber which should be very short.

When the instrument is in operation all of the upper part of the apparatus (*C t*) is filled with carbonate of soda in order to prevent coagulation of the blood. The level of the mercury is (*n*) in the bottle, and (*n'*) in the small tube. This level corresponds to zero, and when the blood presses on the surface of the mercury the pressure is communicated by the opening (*T*) of the iron tube and the mercury ascends in the graduated glass tube. The length of the tube (*T*) should be as great as 250 millimetres for powerful pressures. (Bernard, "Propriétés et altérations des liquides de l'organisme, tome i., p. 167.)



Experiments XIX. and XX. show that when the pneumogastrics are divided and the action of the heart is accelerated its force is diminished as measured by the cardiometer; and that when the action of the heart is retarded by a feeble current of electricity its force is correspondingly increased. Both the arterial pressure and the pulsations are diminished in Experiment XIX. by the administration of ether and very much diminished in Experiment XX. by the operation

of opening the chest; but my object was merely to obtain the relative pressure and pulsations, and the effects of the ether and opening the chest did not interfere with these observations, in which I wished to show that when the pulsations of the heart were increased in number their force became diminished, and *vice versâ*.

The following experiments were made in order to determine the influence of curara on this peculiar action on the heart of electric stimulation of the pneumogastriacs:

EXPERIMENT XXI.—A large dog was poisoned with curara and the heart exposed in the usual way. The pneumogastric nerves were then isolated and a current of electricity passed through them. The apparatus was the one used in the other experiments; and with the most powerful current that could be produced it was impossible to affect the action of the heart. The animal had come completely under the influence of the curara.

EXPERIMENT XXII.—A large turtle was poisoned with curara at 1 P. M., and at 4 P. M. was quite dead. The heart was exposed and found contracting regularly. The pneumogastric nerves were then isolated in the neck and a powerful current applied with the machine before mentioned. It was impossible to arrest by this means the action of the heart.

These experiments, like Nos. XVII. and XVIII., illustrate many others of a precisely similar character.

The experiments here detailed confirm the facts that electric stimulation of both pneumogastriacs will arrest the movements of the heart and that curara so affects these nerves as to abolish this action. This action of curara on the motor filaments is similar to its action on other motor nerves. Having an opportunity of operating upon the alligator and wishing to repeat these experiments and to observe, at the same time, the action of curara upon this animal, I did so with the following interesting results:

EXPERIMENT XXIII. November 14, 1860.—An alligator more than six feet long was poisoned by the injection of about three grains of curara under the skin of the hind leg. This curara was of an inferior quality, and the dose was equal to about a grain of that made use of in former experiments. In thirty minutes he came sufficiently under its influence to be easily handled. The chest was then opened and the heart, which was pulsating regularly, exposed. The animal was quite dead by the time the dissection was finished. The pneumogastric nerves were then exposed in the neck and the electric current was applied. The movements of the heart were arrested so long as the current was continued

and began again when it was interrupted. Artificial respiration was kept up for some time, but this had no effect upon the action of the heart and was done merely to exhibit the play of the lungs. The animal was kept under observation three or four hours and the foregoing fact was repeatedly verified.

EXPERIMENT XXIV. January 28, 1861.—The above experiment was repeated upon another alligator of about the same size as the first but poisoned with the best quality of curara. In making the dissection for exposing the heart, a small nervous filament going to the sterno-mastoid muscle was exposed, irritation of which with the scalpel induced contraction of the muscle, though the animal was quite dead. The pneumogastric nerves were exposed and the heart's action arrested by a moderate electric current. The animal was kept under observation more than three hours and this point was repeatedly verified.

Twenty-four hours after, the heart was still beating vigorously and could be arrested as before. The nervous filament going to the sterno-mastoid muscle was stimulated, which produced slight contractions of the muscle. Muscular irritability was very marked.

It is only in birds that experimenters have met with any peculiarity in regard to the influence upon the heart of electric stimulation of both pneumogastric nerves; and in proportion to their elevation in the animal scale, it has been difficult, and in most cases impossible, to arrest the action of the heart by the means which will invariably produce this effect in mammals, and more easily, even, in cold-blooded animals. Nor have any animals been found able to resist the influence of the curara upon the motor nerves, with the exception of the alligator. These observations should be extended to alligators of small size; but as yet I have not been able to procure them.

When I first noticed the phenomenon which I have described, I was at a loss to account for it; for the alligator was motionless and insensible and the curara had been tolerably prompt in its action, the animal coming under its influence in thirty minutes to three-quarters of an hour or an hour; which, in a large cold-blooded animal, where the processes of life are languid, is as soon as one would expect. In carefully reviewing, however, my observations, I found that in the alligator the nervous system was much less affected by curara than in other animals. In dogs the motor nerves become entirely paralyzed and death takes place by arrest of the muscles of respiration; while in the alligator, when voluntary movement and the cerebral functions are abolished so that the animal can be operated upon

without the slightest difficulty, the motor nerves still respond to stimulation. In Experiment XXIV. a nervous filament was exposed during the operation and still retained its irritability, as shown by muscular contractions when it was irritated with the point of the scalpel. This persisted and was marked, though in a less degree than before, twenty-four hours after death. The properties of the pneumogastrics remained with no sensible diminution.

It is evident that the motor properties of the pneumogastric nerves, especially the branches distributed to the heart, are more important to life than those of ordinary motor nerves distributed to the general muscular system; and it appears that this nerve is protected from disturbing influences, like the action of poison, to a greater degree than others. Evidence of this is seen in the various sources from which the pneumogastric derives its motor filaments; anastomosing, as it does near its origin, with the spinal accessory, the facial, the sublingual and the first and second cervicals. Not satisfied, however, with this purely anatomical explanation, I endeavored to determine its powers of resistance to poisonous agents experimentally. To do this I tried to find some means of retarding the absorption of curara, observing its effects upon the nerves of the animal from the first, to determine whether its action upon the general motor system precedes that upon the pneumogastric nerve. For this purpose I made the following experiments, observations on the alligator not being in themselves satisfactory:

EXPERIMENT XXV. February 1, 1861.—A medium-sized dog was etherized and the chest opened in the usual way. The operation was done at 2.15 P. M., and at 2.40 a grain of curara dissolved in water was injected under the skin of the thigh. The sciatic nerve and both pneumogastrics were then isolated and stimulated. By this means, convulsive movements were produced in the leg and the heart was promptly arrested by a feeble current.

At 3.10 the sciatic and pneumogastrics were stimulated, producing convulsions in the leg, not so marked as before, and arresting the action of the heart.

At 3.40, one hour after the injection of the curara, the sciatic was found inexcitable, but the heart could be arrested by stimulation of the pneumogastrics, though it required a powerful current. A weaker current diminished the frequency and increased the force of its pulsations.

At 4.10 the sciatic was still inexcitable but a powerful current applied to the pneumogastrics arrested the action of the heart.

EXPERIMENT XXVI. March 11, 1861.—One grain of curara of an inferior quality dissolved in water was injected under the skin of a medium-sized dog. Twenty-five minutes after, no effect being produced by the first injection, a second grain was introduced. In ten minutes signs of poisoning were manifested, the posterior extremities became partially paralyzed and the animal was placed upon the operating table. The chest was then opened and the heart exposed, the animal giving no evidence of pain. The pneumogastric nerves were then isolated and stimulated, promptly arresting the action of the heart. After the observation had been continued for about thirty minutes the animal partially recovered from the influence of the curara and made some voluntary movements.

Aided by these experiments, it is easy to understand why, in the alligator, stimulation of the pneumogastrics continued to arrest the action of the heart when the animal had been poisoned with curara. The alligator when undisturbed breathes very slowly; and as in other cold-blooded animals, pulmonary respiration is not necessary to the movements of the heart. Curara seems, then, to act first upon the brain, abolishing voluntary motion, before the motor nerves are paralyzed. This was demonstrated in Experiment XXV. on the dog; for the effects of the ether which was administered before making the dissection were allowed to pass off, and the curara which was subsequently administered abolished voluntary motion long before the motor nerves were much affected, as demonstrated by stimulation of the exposed sciatic. The general motor nerves then slowly came under its influence, and last, the pneumogastrics, although their action on the heart was not entirely abolished. By the means employed in this operation, injecting the curara after the vital powers had been enfeebled by opening the chest and exposing the thoracic organs to the cold air, the dog was approximated to the condition of the alligator.

In Experiment XXVI., an inferior quality of curara was employed, which apparently abolished sensation and volition but had not sufficient power to entirely paralyze the general motor nerves and had little or no effect upon the pneumogastrics. The specimen used had the well-known properties of ordinary curara but was deficient in strength.

From these observations the following seems to be the

action of curara upon the nervous system: It affects volition and sensation, in whatever part of the central nervous system these functions reside, and the motor system of nerves. In regard to the order in which various parts are affected, first, sensation and voluntary motion come under its influence; then, the general motor system of nerves; and last, as the preceding observations have demonstrated, the motor filaments of the pneumogastric nerves, especially those which affect the heart. By an ingenious series of experiments with this substance upon frogs, Bernard has demonstrated the fact that curara affects the motor nerves exclusively, leaving the sensory filaments intact as well as the muscular system. He has also shown that the sympathetic system is paralyzed; for the abnormal heat and congestion which are developed in the ear of the rabbit, for example, when the sympathetic is divided, and which are reduced to the normal standard when the cut extremity is faradized, are abolished when the animal is put under the influence of this agent.*

In the beginning of the section devoted to the influence of the pneumogastrics upon the heart, I mentioned that although the phenomena which follow stimulation of this nerve are well established, no explanation of them has yet been given which is generally accepted. Many theories have been offered by physiologists, but it is not my object to discuss them here. I shall endeavor simply to give the actual state of knowledge on this subject, derived from the experiments detailed in this essay and others which are generally accepted.

I. The heart possesses in its own fibres the property of intermittent contraction, and the stimulus of the blood passing continually through its cavities regulates to a certain extent its movements. This is shown by experiments in the section on the "Cause of the Rhythmical Contractions of the Heart." Observations on the heart after section of both pneumogastrics in the neck show that these nerves further regulate the heart's action; for when their influence is cut off, the pulsations of the organ become rapid and feeble. This is shown in Experiment XIX., in

* For a full exposition of these facts, the reader is referred to Bernard's "*Leçons sur des substances toxiques et médicamenteuses*," and the "*Physiologie et pathologie du système nerveux*."

which the pneumogastrics were divided in the neck, increasing the rapidity of the heart's action but diminishing the force of its contractions, as indicated by the cardiometer. Many instances of palpitation of the heart undoubtedly may be referred to a deficiency in proper innervation transmitted to it through the pneumogastrics; for most of them are due to derangements of the nervous system, and frequently these derangements have their origin either in the lungs, from the individual being put "out of breath" by exercise, or in the stomach, from indigestion, both being organs abundantly supplied with filaments from the pneumogastric nerves. The phenomena which accompany palpitation of the heart are precisely those which are produced by section of these nerves.

II. When the pneumogastrics in the neck are stimulated, the electric current itself is not conducted by the nerves, but there is a stimulus, resembling the ordinary "nerve force," which is conveyed to the muscular fibres of the heart. It is difficult, when the irritability of the pneumogastrics is unaffected, to regulate the stimulus so as to observe the effects of slight action of these nerves upon the heart, its muscular tissue being extremely sensitive to irritation of any kind; but by the action of curara, when it partially paralyzes the nerves, as in the alligator, or in the dogs used in Experiments XXV. and XXVI., it can be shown that a slight stimulus diminishes the frequency but increases the power of the contractions of the heart, while a powerful stimulus paralyzes the muscular fibres. Experiments XIX. and XX. show that when the number of the pulsations of the heart is diminished their force is increased. If electricity is applied directly to the heart, we can equally paralyze its fibres; and in this instance, if the current is sufficiently powerful, this is permanent and no further regular contractions occur. The heart, like other organs, is subject to various changes in its nutrition; and if it were not under the control of and regulated by the pneumogastric nerves, it would be subject to variations in its action which would seriously affect the general system. A certain amount of nerve-force, like the "muscular sense" which produces tonicity of the muscular system, is continually supplied to it by the cerebro-spinal system, which regulates and moderates its action; this can be close-

ly imitated by electricity; a slight current merely moderates the action of the heart, but a powerful current, which represents the nerve-force in an intensely exaggerated form, arrests its action completely. It is not surprising that an organ which possesses such peculiarity in the properties of its muscular structure and the proper action of which is so important to the well-being and the life of the animal should be thus guarded by the nervous system. There are instances on record of immediate death by stoppage of the heart from fright, anger, grief and other severe mental emotions which operate powerfully on the nervous system. Syncope from these causes is by no means uncommon. In the latter instance, when the heart resumes its functions, the nervous shock carried along the pneumogastriacs has been sufficient only to temporarily arrest the action of the heart; in the former, when death is the result, the shock has been so great that the heart is unable to recover from its effects.

MECHANISM OF THE CLOSURE OF THE VALVES OF THE HEART.—The four ventricular orifices of the heart are provided with valves which permit the blood to flow in only one direction. In some of the inferior animals the auricular orifices, by which the blood passes from the veins into the heart, are provided with valvular apparatus. This is the case in fishes; but in animals which have a double heart and in man, the openings of the great veins into the right auricle and of the pulmonary vein into the left auricle are not provided with valves. These orifices are narrowed, however, by the contraction of the fibres during the auricular systole, moderating, though not entirely preventing regurgitation; while the play of the auriculo-ventricular valves permits the blood to flow freely in and fill the ventricles. The ventricles then contract powerfully, close the auriculo-ventricular valves, force open the semilunar valves and project the blood, on the one side, into the pulmonary artery, and on the other into the aorta; from whence it is immediately prevented from regurgitating by the closing of the aortic and pulmonary valves. Thus the blood, forced into the right auricle from the veins of the system, moves in but one direction toward the aorta and is prevented from taking a backward course by

the valves which protect the orifices of both ventricles. It is correctly stated by physiological writers that the tricuspid valves, unlike the mitral, do not always completely close the right auriculo-ventricular orifice. This may be observed in a very simple experiment. Taking the fresh heart of any animal, the bullock, for example, cutting away the left auricle and forcing water into the ventricle with a syringe introduced into the aorta, the aortic valves having been previously destroyed, it will be seen that the mitral valve effectually prevents the flow of the water through the auriculo-ventricular opening; and the free borders of valves, the action of which may thus be exhibited, are closely and effectually brought together by the pressure exerted against them. But if an analogous experiment is performed upon the right side of the heart, cutting away the right auricle so as to expose the tricuspid valves and injecting water against them through the pulmonary artery, it will be seen that a slight regurgitation takes place and that these valves do not so effectually close the auricular-ventricular orifice. Mr. T. W. King, in an essay published in "Guy's Hospital Reports" for 1837, pointed out the peculiarity of action of the tricuspid valves and called it the "safety-valve function of the right ventricle." He stated that it was a provision to prevent congestion of the lungs when anything occurred to obstruct the pulmonary circulation; and it is evident that by this means, the delicate tissue of the lungs, in which congestion can not be relieved by anastomoses as in the general circulation, may be protected from injurious accumulation or pressure of blood. The difference between the action of these valves on the two sides of the heart I have repeatedly verified, and it can be easily demonstrated in the manner just described.

The next question which presents itself is the following: By what means are the valves of the heart made to close? This question may be easily answered in regard to the semilunar valves. The blood circulates in the arterial system under a pressure which will support a column of about six feet of water or six inches of mercury. During the flow of blood from the ventricle into the aorta, the power of the heart overcomes this pressure and opens the valves; but when the force of the heart is taken off, the

valves are closed, effectually preventing regurgitation. One would naturally suppose that the auriculo-ventricular valves were closed in the same way, by backward pressure; and this, indeed, is the general opinion; but in 1843, Baumgarten endeavored to prove by experiment that these valves are closed by a current in another direction, attributing it to a contraction of the auricles and not the action of the ventricles. I do not know that this view has met with much favor, but some observers have confirmed his experiments, and the explanation has been adopted by Milne Edwards * and a few others. The experiments upon which this view is based are briefly these:

The heart of a large warm-blooded animal is prepared by completely removing the auricles so as to expose the auriculo-ventricular valves. It is then held in a vertical position, the valves lying in the cavity of the ventricles, leaving the orifice patent. If water is poured slowly into one of the ventricles through this opening, the valves will gradually float out and their edges approximate; then, when the ventricle is nearly filled, if the stream is suddenly increased in power, the valves completely close.

The facts here stated are entirely correct, and I have repeatedly verified them; but if, as before stated, a stream of water is forced against the valves, the orifice is closed. One can not, therefore, reason from the experiments of Baumgarten that this is the natural mechanism of the closure of the valves, but it is necessary to examine the conditions as they exist in the normal relations of the organ. For that purpose, and with the object of settling this question if possible, I carefully repeated the experiments of Baumgarten and carried his observations a little farther.

EXPERIMENT XXVII. January 30, 1861.—In this experiment I found that the mitral valves were closed when the current of water poured into the ventricle flowed in a small stream. In this case it is evident that they were closed by backward pressure; for the current of water, flowing thus in a bullock's heart prepared in the manner above described, did not exert pressure upon the whole of the auricular face of the valves, but merely made a small opening for itself between them. I then used a larger stream, and in this instance the valves were overpowered, and the water flowed in a full stream from the aorta. The aortic opening was then

* Milne Edwards, "Leçons sur la physiologie et l'anatomie comparée de l'homme et des animaux," tome iv., p. 30.

closed and regurgitation took place freely at the auriculo-ventricular orifice. In this modification of the experiment, however, the force of the water was considerably greater than that of the natural current of blood. It was impossible, indeed, to graduate this, and to pour the fluid into the ventricle in a stream which would impinge upon the entire surface of the valves, which did not flow with considerable force. These facts were repeatedly verified in this, and in confirmatory experiments which it is unnecessary to detail here.

We may now consider the pressure of the blood in the cavities of the heart during circulation; for it is evident that when the auricle is entirely removed and water is poured from a height into the ventricle, the experiment is far from fulfilling the natural conditions, which it is so necessary to observe in all physiological observations. During the normal circulation, the veins, heart and arteries are completely filled with blood; no air or gas can exist, except in solution, in the circulatory system; and especially in the heart does the presence of any gaseous fluid disturb the circulatory function. The blood, also, circulates under a certain pressure; and a certain force is exerted by the heart at every pulsation. In the arterial system the pressure of the blood is represented by a column of six inches of mercury. This pressure is nearly constant in the arteries but is intermittent in the heart. In the heart the pressure is nil during diastole, as has been shown by actual experiment,* but nearly one-third greater than the arterial pressure during its systole. In the venous system the pressure is much less constant than in the arteries; it is always less, and subject to frequent variations. Bernard found the arterial pressure in the carotid of the horse, measured by the cardiometer, to be 110 millimetres. At each cardiac pulsation it was increased to 175.† In another horse he found the pressure in the jugular to vary between 105, 100, 95 and 90 millimetres.‡ The pressure exerted by the contraction of the auricles has not been ascertained; and although it adds something to the venous pressure, it can not be very considerable. Under these conditions, during the diastole of the ventricles, the venous pressure operates upon the auricular face of the auriculo-

* Bernard, "Leçons sur les propriétés physiologiques et les altérations pathologiques des liquides de l'organisme," tome i., p. 173.

† Bernard, *op. cit.*, p. 172.

‡ Bernard, *op. cit.*, p. 203.

ventricular valves, it has no cardiac pressure to oppose it and the orifice is kept patent. The same is true during the contraction of the auricles; the pressure is thereby increased, it is exerted by a column of blood which impinges upon the entire surface of the valves and the ventricles are thus completely filled. During this time the blood is prevented from regurgitating from the aorta and pulmonary artery by the semilunar valves, which are closed by the arterial pressure. But when the ventricles act, they exert a force sufficient to overcome the arterial pressure, which keeps the semilunar valves closed; and at the same time they close the auriculo-ventricular valves, producing one element of the first sound of the heart. The systole of the ventricles ceases; its pressure is taken off; the arterial pressure closes the semilunar valves, producing the second sound; the venous pressure opens the auriculo-ventricular valves, and keeps the orifice patent, until the succeeding contraction of the ventricles. Thus it is that the cardiac pressure, intermittent and operating during the systole of that organ, being greater than the arterial and venous pressure, at the same time opens the semilunar and closes the auriculo-ventricular valves.

Inasmuch as Baumgarten's experiments showed that the auriculo-ventricular valves, which are closed by means of a backward pressure during the systole of the ventricles, can be closed by pouring a stream of water into the ventricles from the auricles, it occurred to me to extend these observations to the aortic semilunar valves, and for this purpose I made the following experiment:

EXPERIMENT XXVIII. January 30, 1861.—A bullock's heart was prepared so as to show the action of the aortic valves; which was done by cutting away a portion of the left ventricle so as to expose them to view, securing the nozzle of a large syringe in the aorta and forcing water toward the ventricular cavity. The semilunar valves were thus closed, effectually preventing the passage of the fluid. While the nozzle was yet in the aorta, diminishing but not preventing the flow of liquid, water was poured from a considerable height into the vessel. The valves were at first floated out and then closed in the same manner as in Experiment XXVII. on the mitral valves. This observation was repeatedly verified.

This last experiment would go as far to prove that the semilunar valves are closed by a current from the ventricle into the aorta, as the preceding one does that the

current from the auricle to the ventricle closes the mitral valves; yet, I venture to assert, no one could entertain for a moment the view that the force which overcomes the resistance of the aortic valves, by operating from the ventricles, closes them by the same current. The experiment, of course, proves nothing in regard to the action of the valves at the aortic orifice, but it shows the falsity of conclusions drawn from experiments in which natural conditions are so utterly disregarded as in those which favor the idea that valves arranged for the purpose of permitting the flow of blood in one direction and preventing reflux are closed by the opposite current.*

SEAT OF THE SENSATION OF THE "BESOIN DE RESPIRER," WHICH GIVES RISE TO THE MOVEMENTS OF RESPIRATION.—The circulation of the blood is intimately connected with the function of respiration. In health the number of pulsations of the heart bears a definite relation to the number of the respiratory movements; when the pulse is increased in frequency, the breathing is more rapid; and when the heart labors, as in cases of advanced disease of this organ, the patient experiences a sense of suffocation which is not dependent upon the condition of the respiratory organs. What gives rise to this sense of suffocation? Why is it, when the lungs are unaffected and when a large supply of pure air is taken in at every respiratory act, that a sense of suffocation attends imperfect action of the heart? These are questions which are of great interest to the pathologist; but they can not be answered without a knowledge of the seat of sensation of want of air, which ordinarily is not perceived by the brain but insensibly induces respiratory movements, and when circulation or respiration is much disturbed, gives rise to the distressing sensation of suffocation. To resolve these questions, which are as yet imperfectly or incorrectly answered by physiologists, is the object of this division of the present paper.

Respiratory movements are regarded as reflex, a cer-

* Since this paper was written, I have seen a short article on the method and time of closure of the auriculo-ventricular valves, by Dr. Halford; but the experiments seem to prove nothing beyond those here mentioned, being, indeed, little more than repetitions.

tain impression being conveyed to the respiratory centre, followed by the action of the inspiratory muscles. This is partly under control of the will; but under ordinary circumstances is involuntary. It is unnecessary to enter into any discussion in regard to the seat of the respiratory centre. Physiologists now agree that it is situated in the medulla oblongata at about the origin of the pneumogastric nerves. Almost the same unanimity exists in regard to the localization of the impression which gives rise to the inspiratory acts; attributing it to an impression made upon filaments of the pneumogastric nerves by the carbonic acid in the air-cells. This is the view which was advanced by Marshall Hall and which is now generally adopted; but there are difficulties in the way of explaining all the phenomena which are observed in health and disease on this theory. In diseases of the heart there may be dyspnœa, and yet the air be rapidly and efficiently changed in the lungs. The evolution of a large quantity of carbonic acid by the lungs, if it is promptly exhaled, does not produce dyspnœa. In experiments upon the lower animals, which are to be mentioned hereafter, phenomena are developed for which such an explanation will not suffice. There are some physiologists, indeed, who do not accept this explanation of Marshall Hall; among them are Bérard, who locates the sense of want of air in the heart; * John Reid, who thought that the respiratory movements were due to the action of the black blood upon the medulla oblongata; Volkmann and Vierordt, who thought that these movements were reflex and due to the excitation of the general sensory system of nerves by venous blood. This is a question, however, which may be settled by direct experiment.

If a dog is rendered insensible by ether and the chest opened, artificial respiration being kept up by a pair of bellows, he will make no respiratory movements so long as respiration is carried on artificially; but soon after respiration is stopped, the diaphragm, intercostals and other inspiratory muscles, which are actually denuded and exposed to view, will be seen to contract violently, this contraction, or effort at respiration, ceasing so soon as artificial respiration is resumed.

* Bérard, "Cours de physiologie," tome iii., p. 523.

An experiment analogous to this was performed in 1664, by Robert Hooke, in which he demonstrated that respiratory efforts ceased in an animal so long as the requisite quantity of air was supplied to the lungs. In this experiment he made an opening into the pleural cavity and the lungs of a living dog and forced a current of air through the trachea and out at the artificial opening. So long as the current was continued the animal remained quiet; but when it was interrupted he made efforts at respiration. This experiment is made use of by Marshall Hall to support his doctrine of the reflex character of respiration, the excitation coming from the lungs; for, he says, so long as fresh air was supplied to the lungs there was no stimulus for respiration and therefore no efforts were made; but when this current ceased or when carbonic acid was substituted for atmospheric air, the contact of the carbonic acid, which, in the one instance, was exhaled by the venous blood, and in the other was introduced into the lungs, produced the excitation which was necessary to the respiratory act. This, however, is but a superficial view of these phenomena. It is necessary to examine into the condition of the heart and the rest of the circulatory system. It is well known that the heart's action is dependent upon respiration and that an arrest of the interchange of gases in the lungs is immediately felt by the circulation. It was for the purpose of observing these conditions that the following experiments were made:

EXPERIMENT XXIX. February 16, 1861.—A medium-sized dog was etherized and the heart and lungs exposed in the usual way. A pair of bellows was introduced into the trachea and artificial respiration kept up. So long as this was performed, the animal made no efforts at respiration, even after he had almost recovered from the effects of the anesthetic; but when the artificial respiration was stopped, he soon began to make efforts to breathe, as was indicated by contractions of the diaphragm and intercostals, which were exposed to view. The femoral artery was then isolated and divided, a ligature applied to the distal end, and the cardiac end compressed with the fingers so that the blood could be permitted to flow at will. A small stream was then allowed to escape, which was of the brilliant red color of arterial blood, the animal remaining quiet and respiration being kept up actively. Respiration was then stopped, and the animal remained quiet until the blood became dark in the exposed artery. He then, and not until then, began to make efforts at respiration. Respiration was now resumed

and the blood gradually became red. The animal continued to make efforts at respiration until the blood became red in the artery. This observation was frequently repeated and the above phenomena were invariable. Since that time, also, I have repeated the experiment upon other animals, always with the same result.

EXPERIMENT XXX. February 19, 1861.—A good-sized dog was poisoned with curara and the chest opened in the usual way. When the animal came fully under the influence of the poison he ceased all respiratory movements. Artificial respiration, however, was kept up for three hours; and in about two and a half hours he had so far recovered from the effects of the poison as to make efforts at breathing when artificial respiration was interrupted. The femoral artery was then opened and divided as in the former experiment. When respiration was arrested the animal made efforts to breathe, but only when the blood became dark in the artery, and ceased these efforts when it became red again on resuming respiration. This observation was made repeatedly.*

EXPERIMENT XXXI. February 15, 1861.—In a large dog under the influence of ether, in which the heart was beating regularly, the organ was suddenly cut from the chest. The animal afterwards made several respiratory movements. In this instance the "besoin de respirer" could not be derived from the heart, as it had been removed from the body.

EXPERIMENT XXXII. March 11, 1861.—A good-sized dog was etherized and the heart exposed in the usual way. Artificial respiration was actively kept up, and while the heart was pulsating regularly and vigorously, it was cut from the chest by a single sweep of the knife. The lungs were still regularly inflated, but in thirty seconds the animal began to make efforts at respiration, which were continued for two and a quarter minutes. These efforts were powerful and convulsive.

It would seem settled by these experiments, that the "besoin de respirer," which is conducted to the respiratory centre and excites the movements of respiration, is not situated in the lungs or in the heart but in the general system; and the sense of suffocation is due to the presence of black or venous blood in tissues which should be supplied with arterial blood. One would therefore expect that this peculiar sensation would, if it resided in the general system, be conveyed to the nerve-centres by the ordinary sensory nerves and not by the pneumogastrics, as was sup-

* This experiment has additional interest as confirming the well known experiments of Brodie, in which he demonstrated that in poisoning by certain substances, their effects will pass off if artificial respiration is continued for a certain time. Among these poisons are curara and opium. Of course, in this instance, it would have been impossible to preserve the life of the animal after the chest had been opened and the thoracic organs exposed, but he evidently recovered considerably from the effects of the poison.

posed by Marshall Hall. This, indeed, is the fact, as is shown by the following experiment:

EXPERIMENT XXXIII. February 15, 1861.—A medium-sized dog was etherized and the heart and lungs exposed in the usual way. The occurrence of respiratory efforts when the blood became black in the arteries and their cessation so soon as it regained its red color were noted. The pneumogastric nerves were then isolated in the neck and divided, producing the usual effect upon the movements of the heart. The experiments of arresting artificial respiration and exciting respiratory efforts on the part of the animal were then repeated with precisely the same effect as before division of the pneumogastrics and as observed in other experiments.

Although the sense which induces respiration is thus located in the tissues and it is shown that it does not reside in the organs of respiration themselves, the cause of this impression does not appear. The venous blood either irritates the system from the presence of elements which are not contained in the same proportion in arterial blood or the tissues feel the want of some principle which the venous blood does not contain in sufficient quantity. The great difference between venous and arterial blood is in the quantity of oxygen which they contain. According to the latest experiments of Bernard in regard to the comparative quantity of oxygen in arterial and venous blood, it appears that the arterial blood of a healthy dog contained 18.28 parts of oxygen for every hundred parts of blood, while venous blood contained only 8.42 parts of oxygen per hundred.* In these experiments Bernard found that when the gas was estimated by displacement with hydrogen or nitrogen, it became diminished if allowed to stand a few hours, and that part of the oxygen became united with carbon to form carbonic acid. He employed carbonic oxide as a displacing agent, which prevented this change; hence the large proportion of oxygen which he found in both varieties of blood. The usual estimates are based upon the experiments of Magnus and indicate in the arterial blood of five animals (three horses and two calves) separately examined, a mean of 2.44 per cent. of oxygen for arterial, and 1.15 per cent. for venous blood, an estimate very far short of the truth. The venous blood is sup-

* Bernard, "Leçons sur les propriétés physiologiques, et les altérations pathologiques des liquides de l'organisme," tome i., p. 367.

posed by Brown-Séquard and others to be an active stimulant to the tissues on account of its irritating properties; but when it is shown that the arterial blood contains such a large proportion of oxygen, which is indispensable to the system and is contained in small quantity in the non-arterialized blood, the immediate inquiry is as to whether the excitation in question is due to the stimulating properties of the venous blood or the want of oxygen in the tissues, which latter can be supplied only by arterial blood. This question I conceive can be settled by experiment. An animal does not feel the "*besoin de respirer*" while artificial respiration is kept up actively; but he does soon after this process is interrupted. In this case, partially oxygenated blood circulates in the arteries and is supplied to the systemic capillaries. If it be that the tissues simply need oxygen, any cause which would prevent oxygen from coming in contact with them would give rise to respiratory movements, though there is no black blood in the arteries and an abundant supply of fresh air is introduced into the lungs. The following experiment bears upon this point:

EXPERIMENT XXXIV. February 19, 1861.—A good-sized dog was etherized and the chest opened in the usual way. Artificial respiration was established and Experiment XXIX. verified. The blood was then allowed to flow freely from the femoral artery while artificial respiration was actively continued. While the blood continued to flow the respiratory muscles were carefully observed. During the first part of the bleeding, no respiratory efforts took place; but when the blood had flowed for a considerable time and the system was becoming drained, respiratory efforts began, feeble at first, but as the bleeding continued, becoming more violent until the whole muscular system was affected with convulsive movements.

This experiment is of great interest and importance. By the withdrawal of blood while respiration was active the tissues were deprived of oxygen by a diminution in the quantity of blood, and were relieved from the stimulation of the black blood, if it has any stimulating properties, for all the blood going to the capillaries was purely arterial in character. No stimulation, then, was applied to the tissues; they simply were deprived of their normal supply of oxygen by a diminution of the oxygen-carrying fluid. This gave rise to the "*besoin de respirer*," first to a slight extent, but as the hemorrhage continued, increasing in intensity till the whole muscular system was convulsed

from the overpowering sense of suffocation; a sense which is referred to the lungs but which really resides in the general system.

These experiments give a new view of the "besoin de respirer," which gives rise to the respiratory movements, and of the sense of suffocation, which is incident to the interruption of these movements. More and more as knowledge of the functions of the body advances are certain sensations which seem to come from special organs actually located in the general system.

In treating of the sensation now under consideration I am led to compare it with various others that are familiar. The system needs periodical rest; it is undergoing an incessant waste which must be supplied by food, and a continual loss of fluid which must be supplied by water; and it needs a constant supply of oxygen, which is furnished by respiration. These are wants of the general system; but their indications are referred to particular parts. Drowsiness is indicated by drooping of the eyelids; hunger, by uneasiness in the stomach; thirst, by dryness of the mouth and fauces; and the "besoin de respirer" and sense of suffocation, when respiration is interfered with, is referred to the lungs. But the sensation of hunger does not reside in the stomach, though it may be momentarily arrested by the introduction of substances, even of an indigestible character, into its cavity. In a patient suffering from any disease which is characterized by deficient digestion and assimilation, while the system is capable of feeling the want of nourishment, an abnormal appetite is a characteristic symptom; and the hunger is not appeased for any length of time by the introduction of food into the stomach. This, as is well known to practical physicians, is a frequent symptom of diabetes and chronic diarrhœa. Direct experiments have been made upon the sensation of thirst. Magendie and Bernard kept horses without water for twenty-four or forty-eight hours, divided the œsophagus so as to divert food and water from the stomach, and then allowed them to drink. As fast as the water was swallowed it flowed out at the wound; and though the mouth and fauces were moistened, the thirst was not satisfied and the animals continued to drink. Bernard has made similar experiments on dogs in which he had established gastric

fistulæ. These experiments I have frequently repeated, and as they are very striking and easy of execution, I report an example:

EXPERIMENT XXXV. November 17, 1860.—A dog that had been operated upon for the establishment of a gastric fistula two days before was kept without water for twenty-four hours. At the time of the experiment he was quite lively, having suffered little from the operation. The cork was then removed from the tube in the stomach and the animal was allowed to drink. He drank until he desisted from actual fatigue, and after resting for a moment drank again in the same way, the fluid all this time flowing freely from the fistula. This was repeated several times until the animal gave up the effort. The cork was then replaced in the tube, and when the animal drank his thirst was soon satisfied.

These experiments, which are well known to physiologists, show that thirst is a sensation felt in the tissues but referred to the mouth and fauces; and although these parts and the walls of the stomach may be continually moistened, the thirst is not appeased, nor can it be until the fluid has been taken into the blood-vessels and circulates in the system. This desire for liquids is always shown by animals after the withdrawal of blood. I have repeatedly observed animals from which I had removed blood by the jugulars go to the water and drink copiously so soon as they were set at liberty.

CONCLUSIONS.—Respiration is a reflex phenomenon under ordinary conditions; and movements connected with it are due to an impression conveyed from the general system to the medulla oblongata, whence a stimulus is sent out which animates the inspiratory muscles. While respiration is carried on effectually without exertion on the part of an animal, as in artificial respiration, evidently no impression is made upon the respiratory centre, for no respiratory movements take place.

The impression which excites respiratory movements is received from the tissues and not from the lungs; for it is only when dark blood instead of red is supplied to the tissues, that the impression is conveyed to the respiratory centre, producing efforts at respiration.

This impression is not transmitted through the pneumogastric nerves but through the general sensory nerves; for there is no difference in the manifestation of respira-

tory movements when the supply of air to the lungs is cut off, if both pneumogastrics are divided.

This impression is due to the want of oxygen in the tissues and not to stimulating properties of the venous blood; for when the supply of oxygen is cut off by abstracting blood from the system, the phenomena observed as occurring during interruption of respiration are marked, though air is supplied in abundance to the lungs.

This impression is not due to distension of the cavities of the heart, as suggested by Bérard; because the heart may be removed from the body of a living animal and the respiratory efforts will occur as in the case of abstraction of blood.

This impression (the sense of want of air, "*besoin de respirer*") when exaggerated constitutes the sense of suffocation; and it, like the sense of fatigue, of hunger or of thirst, has its usual source in the general system, though it manifests itself in the lungs in the same way that fatigue affects the eyelids, hunger the stomach, and thirst the mouth and fauces. They are all indications of wants of the system and can not be effectually relieved by the local effects of anything upon the organs to which they are referred by the sensations.

The necessity for respiration, or for oxygen, then, exists in the tissues; and asphyxia can not be solely applied to arrest of the function of the lungs, but to anything which interferes with the consumption of oxygen by the system. Anything which operates in this way gives rise to a sense of suffocation and afterward to general convulsions if it is carried sufficiently far. Various pathological phenomena which would otherwise be obscure are thus explained. The operation of simple asphyxia by tying the trachea or preventing air from gaining entrance into the lungs induces the sense of suffocation which first gives rise to respiratory efforts more violent than ordinary, and subsequently, to general convulsions. All are familiar with these phenomena however they may be explained.

In poisoning by carbonic oxide there are general convulsions which arise from the sense of suffocation; for this agent so operates upon the blood-corpuscles, that though they continue red they are rendered incapable of performing their function of supplying oxygen to the system.

In poisoning by hydrocyanic acid, when the system is not immediately overpowered by this agent and the muscular irritability destroyed, the blood becomes incapable of supplying oxygen to the system and convulsions ensue as the result of the sense of suffocation.

In death by hemorrhage, convulsions, occurring just before death, are invariable. This also is the result of deficient supply of oxygen to the tissues, and the sense of suffocation is the starting point. This was demonstrated in Experiment XXXIV., in which the animal was bled to death.*

Finally, in all cases where the supply of oxygen is cut off, not from the lungs but from the tissues, a sense of suffocation is the result, and convulsions ensue following violent efforts at respiration.

SUMMARY.—In the foregoing essay, I think I have established the following facts, which are either not generally admitted or not understood by physiologists:

I. That the heart elongates during the systole of its ventricles.†

II. That the cause of the rhythmical contraction of the muscular fibres of the heart is resident in the fibres themselves, is one of their inherent properties and remains so long as they retain their "irritability."

III. That the normal stimulus which excites the regular and efficient movements of the heart is the blood, and that this can not be replaced by a fluid of less density.

IV. That although the flow of blood in the cavities of the heart is sufficient to induce, under ordinary conditions, regular contractions of the organ, still it is necessary that these movements be further regulated and controlled; and that this is effected mainly through the agency of the pneumogastric nerves.

V. That the action of the heart may be arrested through the motor filaments of the pneumogastric nerves by means of electricity; that this does not take place in animals poisoned by curara, on account of the paralysis of the motor nerves. That the motor filaments of the pneu-

* These convulsions have been explained in various ways by physiologists but never satisfactorily, though they have long been observed.

† See foot-note on page 69.

mogastrics are the last which are affected by this agent, and that in the alligator they are left almost intact. That the cause of the arrest of the heart's action by stimulation of the pneumogastrics is an exaggeration of the force which regulates the action of the heart, rendering it slower and more powerful.

VI. That in asphyxia, the cause of the arrest of the action of the heart is overdistension of its cavities; and that anything which brings about sufficient distension will also arrest the action of this organ.

VII. That the auriculo-ventricular valves are closed by a backward pressure operating during the contraction of the ventricles, and not by the current of blood from the auricles to the ventricles.

VIII. That the impression which gives rise to the reflex acts of respiration is received from the general system and not from the lungs or heart. That this impression is due to the want of oxygen in the tissues and not to stimulating properties of the venous blood. That the exaggeration of this impression constitutes the sense of suffocation and gives rise, if excessive, to general convulsions.

APPENDIX

SOME POINTS IN THE ANATOMY OF THE CIRCULATORY SYSTEM OF THE CROCODILUS MISSISSIPPIENSIS, OR ALLIGATOR.—The anatomy of the alligator is imperfectly and in many respects incorrectly described in most works upon Natural History. The description of the circulatory apparatus, however, given by Milne Edwards,* in his work on "Physiology and the Comparative Anatomy of Man and the Inferior Animals," now in course of publication, is quite accurate; and as the arrangement of the heart and larger vessels is peculiar, I have thought that a sketch of these parts might not be uninteresting.

The heart is quite small in proportion to the size of the animal, and like the organ in reptiles generally, the ventricular portion is small in proportion to the size of the auricles. The position, shape, etc., of the auricles do not

* For a full description of the circulatory system of the alligator, see Milne Edwards, "*Leçons sur la physiologie*," etc., tome iii., p. 424 *et seq.*

differ from those in other reptiles, except that the right auricle is much larger than the left; but the ventricular portion is divided by a complete septum into two chambers, a right and a left, like the heart of a warm-blooded animal. From the ventricles arise the two aortæ; one from the left, and one from the right side. There is also a pulmonary artery going to the lungs from the right ventricle. The right aorta passes immediately over to the left side; and as it carries venous blood, it may be called the venous aorta; while the left, or arterial aorta, passes directly over to the right side. There is no communication between either auricles or ventricles upon the two sides; but at the origin of the two aortæ is an opening which permits a mixture of venous and arterial blood to a limited extent. This is called the foramen of Pinazza, because its discovery was formerly supposed to belong to him. It was described by Hentz, an American anatomist, in 1824, in a paper published in the "Transactions of the American Philosophical Society," while Pinazza described it in 1833. Following out now the distribution, etc., of these two aortæ, the arterial aorta first gives off a large branch, the brachio-cephalic, which almost immediately gives off the left subclavian going to the left superior extremity. The brachio-cephalic divides into the left subclavian, already mentioned, and a single carotid artery which goes in the median line to the base of the skull, there divides into two vessels, which soon bifurcate and form the external and internal carotids of the two sides, the internal going to the encephalon, and the external to the muscles, etc., about the head. Next is given off the right subclavian artery, distributed to the right superior extremity. Each subclavian artery, a short distance from its origin, gives off a small cervical artery, which goes to the head and is accompanied by the jugular vein and the pneumogastric nerve. These are the principal branches which are given off by the arterial aorta alone. The venous aorta gives off no branches in the neck, but passes back to the vertebral column, anastomoses by a branch of considerable size with the arterial aorta, and sends a branch, larger even than the anastomosing branch, to some of the abdominal viscera, which are thus supplied with venous blood. The dorsal aorta is formed by the union of the arterial aorta with the anastomosing branch

of the venous aorta, and thus carries mixed blood. It passes down the back, gives off in its course the intercostals, the anterior mesenteric, the renal arteries, the vessels of the posterior limbs, the posterior mesenteric and finally is distributed to the tail.

The distribution of the blood in this animal is peculiar. The forelegs, the head and face are supplied with almost pure arterial blood, as the communication by the foramen of Pinazza is very imperfect. There is but a single carotid artery in the neck, and the pneumogastric nerves are found accompanying the cervical arteries, which are given off by the subclavians. Some of the abdominal viscera, the stomach, liver, spleen, etc., are supplied with venous blood. The kidneys, intestines, hind legs and tail are supplied with a mixture of arterial and venous blood.*

The length of time for which the nervous and muscular irritability in these animals is retained after death renders them very valuable in many physiological experiments. I have found that when poisoned with curara this persisted for days. For a considerable time, four or five days after death, even when the weather was quite warm, no decomposition took place. I do not know that this apparently antiseptic property of curara has ever been remarked, but it certainly seemed to retard decomposition in the alligators upon which I have experimented.

* The description of the heart and arteries, which is here given, is nearly if not precisely according to the views entertained by Dr. Bennett Dowler, of New Orleans, who has made extensive researches into the anatomy and physiology of the alligator. These views, however, have never been fully published by him but were verbally communicated to me.

VI

MECHANISM OF REFLEX NERVOUS ACTION IN NORMAL RESPIRATION

AN ADDRESS DELIVERED FEBRUARY 16, 1874, BEFORE THE NEW
YORK SOCIETY OF NEUROLOGY AND ELECTROLOGY*

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MR. PRESIDENT, AND GENTLEMEN OF THE SOCIETY:
I shall have the honor this evening of making some remarks on the mechanism of nervous reflex action in normal respiration. A great part of the statements that I shall make and the views advanced upon this subject are derived from personal experimentation; but they are not entirely new, for many of the experiments upon which my views are based were published in the "American Journal of Medical Sciences," in October, 1861. Still, these experiments, which seem to me to be of considerable importance, have been noticed so little in physiological writings that I venture to assume that they may be new to many of those who now listen to me.

After Marshall Hall had formularized the ideas of certain of his predecessors in regard to what he termed reflex action, it was pretty generally understood by physiologists that the movements of respiration were of a purely reflex character, unless they were modified by voluntary acts; and that the ordinary movements of respiration, which take place without the intervention of the will, were entirely reflex.

The experiments that I shall detail this evening were based upon, or rather suggested by an experiment made in 1664, by the celebrated Robert Hooke, and published in the "Philosophical Transactions" for 1667. This experiment, though it could not be completely understood

* Phonographically reported by George W. Wells, M. D., of New York.

at the time it was made, in 1664, is very instructive. It consisted in introducing a bellows into the trachea of a dog, making an opening into the chest, cutting off a portion of the lungs and forcing air through them; and it was found that so long as air was forced through the lungs in this way the animal, though sensible, made no efforts at respiration. I may here anticipate enough to say that I shall assume that in this experiment, while air was supplied to the system the animal felt no want of it, had no inclination to respire and consequently did not respire.

In studying the subject of the reflex nervous action in respiration, one is immediately struck with the anatomical relations of the pneumogastric nerves to the respiratory apparatus; and it is all the more important to study the relations of these nerves to the process of respiration, as they arise near that point in the medulla oblongata where the so-called "vital knot," or the respiratory nerve-centre, is supposed to be situated.

It may be opportune, perhaps, to rapidly sketch the condition of knowledge respecting the influence of the pneumogastric nerve upon respiration.

The pneumogastric nerve is one of immensely wide distribution and is connected with various distinct functions. The branches that are distributed to the respiratory organs are the following:

The superior laryngeals, which are distributed to the mucous membrane of the larynx and the membrane covering the top of the larynx, sending off a branch on either side to the crico-thyroid muscle, this branch being a mixed nerve.

Next in order are the inferior, or recurrent laryngeal nerves, which are distributed to all the intrinsic muscles of the larynx except the crico-thyroid. These nerves are composed entirely of motor filaments and are derived from a variety of sources. The experiments of Bernard, which have been so often repeated by Dr. Dalton, myself and others, of extirpating the spinal accessory nerves, or the section of the communicating branches to the pneumogastriks, show that the spinal accessory is the nerve of phonation; and the filaments that preside over the voice pass to the larynx through the recurrent laryngeals.

Then, distributed to the lungs themselves, are the an-

terior and posterior pulmonary branches, which go almost exclusively to the mucous membrane of the pulmonary structure. These branches communicate with the sympathetic; but according to Sappey, they do not go to the walls of the blood-vessels, being distributed to the membrane of the bronchia and the air-vesicles.

So much for the distribution, in general terms, of those branches of the pneumogastrics which go to the lungs; and this distribution being so extensive, one can hardly discuss the reflex nervous action in respiration without taking the action of these nerves into consideration.

The pneumogastric is originally an exclusively sensory nerve. Experiments are somewhat obscure upon this point, on account of the difficulty in irritating the original roots of the pneumogastrics without involving filaments of other nerves; still, the careful experiments of Longet showed that when the spinal cord of animals is opened and the roots of the pneumogastrics are carefully isolated and stimulated, no movements follow their irritation. This shows that the original filaments of the pneumogastric are not motor; but as the nerve emerges from the cranial cavity, it receives a number of communicating motor filaments, and thus in its course it is a mixed nerve. Following out the distribution to the respiratory apparatus, it is found that the filaments from the superior laryngeal going to the crico-thyroid muscle are almost exclusively motor; the motor filaments of the recurrences go to the intrinsic muscles of the larynx, whereas the true pulmonary branches are distributed to the mucous membrane. Therefore, excluding the movements of the larynx, the action of the pneumogastric in the reflex phenomena of respiration, theoretically, would be that of a sensory nerve, conveying to the respiratory nervous centre an impression, or sensation, which gives rise to the movements of respiration.

If both pneumogastrics, however, are divided, the respiratory movements are very much diminished in frequency; and I have in my mind an experiment in which they were reduced from twenty-four to four or six in a minute; yet they still continue; and this simple experiment, so often performed as a class-demonstration, is a denial of the proposition that the pneumogastrics are the only nerves for the transmission of the so-called "*besoin de respirer*," or sense

of want of air, to the respiratory nerve-centre. If the pneumogastrics were the only nerves having this function, respiration should cease after their division; but it does not.

I think that physiologists are not at present able to explain the cause of the great diminution in frequency of the respiratory movements after the division of both pneumogastric nerves; but this is, nevertheless, an invariable phenomenon. In the experiment to which I have referred, curiously enough the animal did not die; and when I presented him to my class, about three weeks after the section of the nerves, the number of respirations had returned to the normal standard. I imagine that a reunion of the two ends of the divided nerve had occurred. A post-mortem examination, the animal being sacrificed in another experiment, showed that the nerves, though not, perhaps, completely united, had formed a partial union between the divided extremities.

The condition of the lungs after division of the pneumogastrics—that is, in cases where death follows such division—is peculiar and was for a long time unexplained by physiologists. In animals that live for three or four days and then die, the lungs present pretty generally, throughout their entire substance, a carnified condition. They are solid, will sink in water, but still do not present evidences of inflammation. It was thought at first that this was due to inflammation; but physiologists failed to find the positive evidence of any such process. Bernard, I think, has given the correct explanation of this peculiar appearance. He observed that when the respiratory movements are gradually diminished in frequency they are immensely increased in depth; that the inspirations are remarkably prolonged and profound; and that the chest, in the inspiratory act, is extraordinarily distended. He advanced the idea that this extreme dilatation of the air-cells induced capillary hæmorrhage in certain parts of the lungs; that as this extended, the blood coagulated; and finally, the lungs became almost solid.

Faradization of both pneumogastrics in the neck arrests the respiratory movements, if it is powerful; and this action is reflex, not direct. If the nerves are divided, faradization of their peripheral extremities has no effect on respiration, though it arrests the action of the heart; where-

as faradization of the central ends arrests respiration in the same way as faradization of the nerves before their division. Faradization of the superior laryngeal nerves arrests respiration and renders the animal motionless. This effect follows powerful faradization of any of the sensitive nerves, though not so certainly and promptly as faradization of the superior laryngeals. If the superior laryngeals are powerfully stimulated, respiration stops immediately and is arrested at the instant the current is applied, but more easily during inspiration than expiration. This arrest of the respiratory movements is particularly marked as regards the action of the diaphragm. I have made these preliminary remarks to show that there is very little known in regard to the reflex phenomena of respiration operating through the pneumogastrics.

Although the proposition that I am about to make has been denied by a few physiologists, still, the greater number believe that the medulla oblongata is the respiratory nerve-centre. Adopting this view, which is almost universally accepted, the mechanism of the reflex phenomena of respiration may be briefly stated as follows:

These phenomena require three conditions:

I. The physiological integrity of nervous filaments conveying a certain impression, or sense, to the nerve-centre.

II. The existence and physiological integrity of the nerve-centre.

III. Finally, the physiological integrity of the motor nerves which convey the stimulus that is generated at this nerve-centre to the inspiratory muscles.

If it be assumed that respiration involves a reflex action, it must be admitted that there are nerves which convey certain impressions to the medulla oblongata. The medulla oblongata is the respiratory centre; and when this centre is destroyed, the movements of inspiration instantly and permanently cease. A single series of experiments has been published by Dr. Brown-Séquard, which are assumed to prove that respiratory movements may occasionally persist after destruction of the medulla oblongata; but they have never been confirmed and can not be accepted as demonstrating that the medulla oblongata is not the centre for respiration.

The sensation of want of air has been called by the

French, the "besoin de respirer." It might be well enough to call it, indeed, the sense of the want of air. Under ordinary conditions, when respiration is free and when the surrounding air is pure and in abundance, this sensation is not felt except at the medulla oblongata. This impression, however, at proper intervals is conveyed to the medulla and keeps up the respiratory movements, without our knowledge; and it is only when there is a greater deficiency of air than usual or when there is an obstruction to respiration, that this sense of want of air becomes a positive sensation, in the form of a sense of suffocation, more or less pronounced. I think that the old experiment of Robert Hooke established this point; and it certainly demonstrates it, when taken in connection with what has been learned of late years.

In Robert Hooke's experiment the dog was supplied artificially with air, completely and efficiently; and it was noted that so long as the respiratory needs were supplied, though the animal looked around and was entirely sensible, he made no respiratory efforts. This showed that during the free passage of air through the lungs the want of air was not felt by the medulla oblongata and there was no stimulus to induce respiratory movements. There was no necessity felt for respiratory movements and none took place. This experiment suggested my own observations made in 1861. I put an animal, a dog, completely under the influence of ether, introduced the nozzle of a bellows into the trachea, opened the chest, turned back the anterior walls by breaking the ribs, so that I exposed the lungs and diaphragm, and then very carefully maintained artificial respiration. I found that while artificial respiration was complete and efficient the animal remained perfectly quiet and made no respiratory efforts. I could see in this experiment the slightest movement of the diaphragm. I then interrupted the artificial respiration for a moment. Very soon I could see the diaphragm begin to quiver; it contracted at first slightly; then, more and more powerfully and rhythmically; and the animal finally opened the mouth and made ineffectual efforts to breathe. I then resumed the artificial respiration, and in a short time, when the respiratory needs were entirely supplied, the animal became quiet.

I then exposed an artery and introduced in it a stop-cock, so that I could take blood from the vessel at will. While I kept up artificial respiration, I drew a little blood from the artery upon a white plate. It had all the characters of pure arterial blood. I then had my assistant, who was working the bellows, stop the artificial respiration and I allowed the blood to flow in a small stream from the artery. I found, always and invariably, that when the blood began to be dark in the artery, and not before, the animal made efforts to respire.

There are several views, which have been advanced by physiologists from time to time, as to the location of the "*besoin de respirer*."

Marshall Hall and some others thought that it was due to a want of air in the lungs themselves, and that this want was conveyed by the pneumogastric nerves to the medulla oblongata; but I do not see how, under this supposition, it is possible to explain respiratory movements which occur after division of both pneumogastrics.

Reid thought that the sense of want of air was due to the circulation of venous blood in the medulla oblongata.

Bérard thought that the sense of want of air, or the "*besoin de respirer*," was due to the distension of the left side of the heart by venous blood when respiration was arrested. In support of this view, he brought forward the well-known fact that in certain cases of disease of the heart, even when the lungs are perfectly normal and completely filled with air, there is frequently a sense of suffocation.

Vierordt thought that the sense of want of air was due to the circulation of venous blood in the substance of the nerves themselves.

Volkman, in 1842, made the very important observation that an animal experiences the sense of suffocation when deprived of air after division of both pneumogastrics. This fact was well known. Every one who has divided both pneumogastric nerves in a cat must have noted that the animal experiences intense distress from suffocation. In this animal the cartilages of the larynx are very flexible, and paralysis of both recurrent laryngeal nerves, which follows division of the pneumogastrics in the neck, causes the glottis to close in inspiration, so that the animal is almost immediately deprived of air. Volkmann reasoned

from this fact, which had often been observed before, that the sense of want of air resides in the general system and is not to be referred to any particular organ or organs.

If I may be permitted, now, to continue the account of my own experiments, I think I can show that it is certain that the sense of want of air resides in the general system; and furthermore, that it is due to a want of oxygen in the general system.

Here is an animal with the heart and lungs exposed; a bellows placed in the trachea, and artificial respiration maintained; but there are no efforts at breathing so long as air is supplied in sufficient quantity. Put a stop-cock in the artery, and while artificial respiration is continued, there is the natural red color to the blood. Stop the respiration, however, and just so soon, and no sooner, as the blood becomes markedly dark in the arteries, the animal begins to make efforts at respiration and feels the sense of want of air. I think this experiment shows that the sense of want of air is due to the circulation in the system of blood more or less venous in its character.

What is the cause of this sense of want of air and what are the conditions of the blood that are different from the conditions during efficient artificial respiration! Of course, whatever they may be, these two conditions are present: one, a deficiency of oxygen in the blood that is rendered more or less venous; and another, the presence in the arteries of blood containing an excess of carbonic acid. The question now arises, whether the sense of want of air is due to a deficiency of oxygen in the system or to the irritating qualities of carbonic acid. How can these two conditions be separated experimentally; and how can the tissues be deprived of oxygen without supplying blood charged with carbonic acid! A very simple way is to drain the system of blood; for if blood gets to the system, there is no question that oxygen will be carried to the tissues, it being always conveyed by the blood, and by the blood alone. Therefore, if the system is deprived of blood no oxygen can get to the tissues. Again, if the system is drained of blood by cutting out the heart, the question whether or not the sense of want of air is due to the distension of the left side of the heart by venous blood is answered. Take this same animal, that is not breathing,

the respiration being kept up by the bellows, and tie a ligature around the aorta; he begins to breathe, although the lungs are supplied with air, for the reason that the oxygen-carrying blood is cut off from the system. If, now, in this same animal, the heart is suddenly cut out, the system is of course almost instantly drained of blood; and the animal always makes violent and repeated respiratory efforts, although the lungs are fully supplied with air. It seems to me that these experiments show conclusively that the sense of want of air is derived from the general system; that it is due to a want of oxygen in the system, and not to the irritating properties of carbonic acid; and that this sense is entirely analogous to the sense of hunger and the sense of thirst. The sensations of hunger and of thirst are subjectively referred to the stomach or to the mouth and fauces; but they really reside in the general system. If a fistula is made in the stomach of a dog, and if the animal is allowed to drink, after having been deprived of water for a day or two, the water will flow out through the fistula as fast as it is taken into the stomach; and although the animal will continue to drink, the water is not absorbed and the thirst is not satisfied. I have seen animals drink, in this way, gallons of water, being satisfied with a moderate quantity after the fistula has been closed. Also, if food is taken into the stomach and not absorbed, the sense of hunger is but momentarily appeased; but this sense is referred to the stomach because food is naturally introduced into the system by the stomach. So the sense of want of air, which I believe to be due to the want of oxygen in the tissues, is referred to the respiratory organs because it is by filling the thorax that this deficiency in the system is naturally supplied. If the sense of want of air becomes exaggerated, it constitutes the sense of suffocation; and this is one of the most distressing of sensations.

It has been observed that convulsions very often follow hemorrhage; and this fact has been found difficult of explanation. But hemorrhage is really suffocation; and convulsions are generally observed in suffocation. It makes very little difference, practically, whether the system is drained of the oxygen-carrying fluid or whether oxygen is prevented from going to the lungs; in either case the

same result follows as far as respiration is concerned; and in death from profuse or sudden hemorrhage, it seems to me that the convulsions are in fact no more than convulsions due to suffocation. This view seems to offer a satisfactory explanation of the convulsions following hemorrhage. There is one point, however, in this connection, which is interesting and which I appreciate as fully as any one who now hears me.

I have assumed that draining the system of blood, by preventing the oxygen from getting to the system without carrying to the tissues carbonic acid, proves that the sense of the want of air is due to a want of oxygen in the tissues and not to the stimulation of carbonic acid. Carbonic acid does not originate in the blood, and it is undoubtedly an excretion. A muscle cut from a living frog and put under a bell-glass containing oxygen, even though it contains no blood, will respire. Again, the same muscle in an atmosphere of hydrogen will give off a certain quantity of carbonic acid. In normal nutrition carbonic acid is carried away from the tissues, almost as soon as it is formed, by the blood. If, then, the system is drained of blood, what is to prevent the carbonic acid from accumulating in the tissues, and may not this be the cause of the sense of want of air!

I have tried to imagine experiments to meet this objection. I have tried to devise some means of getting rid of the carbonic acid from the tissues, that will not at the same time either supply oxygen or send through the tissues a fluid like blood, containing carbonic acid. This flaw in my argument I can not correct experimentally.

One other important point in this connection, which may be of more interest to some of my hearers than those to which I have thus far called attention, is the cause of the first respiratory effort made by the newborn child.

Many of the ancient writers regarded the placenta as the respiratory organ of the foetus; and it is now known positively that the foetus in utero gets its oxygen from the blood of the mother through the placental vessels; but when the child is born, this source of supply of oxygen is cut off and the first act of pulmonary respiration is performed, this being the beginning of the function which continues to the end of life.

What is the exciting cause of this first respiration! It has been shown positively, by experiments upon animals, that the first respiration is due to an arrest of the placental circulation. I have frequently opened the abdomen of dogs and cats big with young and taken the young from the uterus, when they had hardly attained one-fourth of their size at term, have laid them on a table, and respiratory movements have always occurred in a very short time after they were separated from the mother. Experiments have been made upon animals, by opening the abdomen and pressing upon the umbilical cord; and in a short time respiratory movements have occurred.

It is well known to gynecologists and obstetricians that respiratory movements occasionally occur in the human foetus in utero as a consequence of some interference with the placental circulation; and the amniotic fluid and even meconium have been found in the respiratory passages.

A very thorough exposition of these facts has lately been made by Dr. B. S. Schultze, in a work published at Jena, in 1871, entitled "*Der Scheintod Neugeborener*," in which the points I have stated are so fully set forth that there can be no doubt upon the subject. It seems to me that the respiratory efforts before birth constitute a very strong argument in favor of the view that I have stated; and it seems to me certain that the first respiratory movements after birth are due to the following conditions: The placental circulation is arrested; the new being feels the sense of the want of air; and the impression is conveyed to the medulla oblongata, where a stimulus is generated which is carried by motor nerves to the inspiratory muscles. The inspiratory muscles then contract, and thus the lungs are for the first time distended with air.

The general results of the experiments that I have detailed this evening, and which, I may say, I have performed over and over again, are the following:

Respiration is a reflex phenomenon. The movements of respiration are reflex. There is a special respiratory nerve-centre, which is situated in the medulla oblongata. When this nerve-centre is destroyed, no respiratory movements can take place, because there is no centre to receive the impression of want of air. Respiratory movements

are due to an impression made upon the centripetal nerves; and this impression is due to a want of oxygen in the general system. The sympathetic system may possibly be involved in this action, but this point has not been determined. The sense of the want of air, conveyed to the medulla oblongata, gives rise, under ordinary conditions, to respiratory movements, which take place without the consciousness of the individual. Under ordinary conditions respiration is carried on by the medulla oblongata and does not involve the action of the brain. Whenever there is any difficulty in respiration, the sense of want of air is exaggerated until it becomes a sense of suffocation, which involves voluntary efforts on the part of the individual to supply the want of air.

VII

EXPERIMENTS ON THE EFFECTS UPON RESPIRATION OF CUTTING OFF THE SUPPLY OF BLOOD FROM THE BRAIN AND MEDULLA OBLONGATA

Published in the "New York Medical Journal" for November, 1877.

IN October, 1861, I published in the "American Journal of the Medical Sciences" a paper on "Points connected with the Action of the Heart and with Respiration." In this paper I contended that the respiratory sense, "besoin de respirer," of the French, or sense of want of air, which gives rise to the movements of respiration, is due to a want of oxygen in the general system. I assumed that in the medulla oblongata is to be found the centre presiding over the respiratory movements; that these movements are reflex; that a certain sense, called the respiratory sense, is conveyed to the medulla oblongata; and that it is this sense which is the starting-point of the respiratory acts. I showed that a dog brought under the influence of ether, with the heart and lungs exposed and with a bellows in the trachea, will make no respiratory efforts so long as air is efficiently supplied to the lungs by artificial respiration, an experiment essentially the same as one made by Robert Hooke, in 1664. In an animal in this condition, I showed that respiratory efforts were made, when artificial respiration was interrupted, so soon as the blood became dark in the arteries, having opened an artery and noted the color of the blood as the experiment progressed.

It seemed to me at that time that the sense of want of air in this experiment was due to the properties of the dark-colored blood circulating in the arterial system; and the question arose in my mind whether this was dependent upon the deficiency of oxygen in the blood or upon the presence of carbonic acid. In order to answer this ques-

tion, I drained an animal (a good-sized dog) of blood by dividing the femoral artery, the chest having been opened with the animal under the influence of ether and artificial respiration being maintained in the usual way. In this experiment, although the lungs were fully supplied with air, violent respiratory efforts were made as the animal became nearly exsanguine.

In another experiment I divided both pneumogastric nerves and ascertained that there was no difference in the phenomena observed, showing that these nerves are not the sole conductors of the sense of want of air. In still another experiment I drained an animal of blood by cutting out the heart. This was followed by violent respiratory efforts, showing that the sense of want of air has nothing to do with distension of the right cardiac cavities.

From the experiments of which I have thus given a brief sketch, made in 1861, I concluded that the sense of want of air, or the respiratory sense, was due to a want of oxygen in the general system, producing an impression which was conveyed to the medulla oblongata and which gave rise to respiratory efforts; that in ordinary respiration, this reflex action took place unconsciously, but became exaggerated when there was a great deficiency of oxygen and was then experienced as a sense of suffocation; that the respiratory sense thus had its origin in the general system and not in the lungs, as the sense of thirst has its seat in the general system, from deficiency of water, and has simply a local manifestation in dryness of the throat and fauces. In addition to the experimental arguments in favor of this view, I saw, in cases of distress in breathing from deficient circulation, as in certain cases of disease of the heart in which the lungs are normal, what seemed to me to be a confirmation of my opinion.

The views which I have just stated were advanced by me in my work, "Physiology of Man," New York, 1866, vol. i., page 479, *et seq.*, and in my "Text-Book of Human Physiology," New York, 1876, page 164, *et seq.* In February, 1874, I made an address before the New York Society of Neurology and Electrology upon the "Mechanism of Reflex Nervous Action in Normal Respiration," an abstract of which was published in the "New York Medical Journal," in April of the same year. The full text of this

address was published in the "Chicago Journal of Nervous and Mental Diseases," in April, 1874. In this I still adhered to my original view, and I extended my reflections to the theory of the cause of the first respiration at birth, respiration in utero by means of the placenta, etc.

At the present day nearly all physiological writers agree that the sense of want of air is due to want of oxygen and not to any stimulating or irritating properties of carbonic acid; and this idea has received confirmation from the experiments of Pflüger upon the effects of respiration of nitrogen, as is seen by the following extract:

"Using bloodletting for ascertaining the condition of the blood during dyspnœa, I arrived at the following facts: As soon as the dog begins to breathe pure nitrogen, it is scarcely fifteen seconds before he makes violent and deep inspirations; at the end of thirty seconds, the most intense dyspnœa is observed, the blood is already almost absolutely black, which must be due to the enormously rapid tissue-metamorphosis of this animal."*

It is seen that this experiment, made in 1868, is almost identical in its idea and results with those which I made in 1861, except that Pflüger made his animal breathe a gas not capable of supporting respiration, while I simply deprived animals of air. Nearly the same experiment as that performed by Pflüger was made by Rosenthal, in 1862, who noted that animals suffered no dyspnœa when air or oxygen was forced through the lungs, but that dyspnœa was manifested when nitrogen or hydrogen was used instead of oxygen.†

While physiologists are now pretty generally agreed that the sense of want of air is connected with a deficiency of oxygen in the blood of the arteries, some writers are of the opinion that the "sense" is primarily due to a want of oxygenated blood circulating in the medulla oblongata. This opinion has been advanced by some authors, but so far as I know it rests mainly upon theory and has no positive experimental foundation. Since I made the experiments which form the basis of this article, I have consulted a number of systematic works upon physiology with refer-

* Pflüger, "Ueber die Ursache der Athembewegungen, sowie der Dyspnœe und Apnœe."—"Archiv für die gesammte Physiologie," Bonn, 1868, Bd. 1., S. 89.

† Rosenthal, "Athembewegungen," etc., Berlin, 1862, S. 4.

ence to the subject under consideration. Most of the works examined contain no very definite allusions to the respiratory sense, or at most only brief and unsatisfactory statements; but in two, I find the following references that are directly pertinent to the question:

"The first respiratory effort of the fœtus is thus produced by the interruption of the placental respiration, the sudden deficiency of oxygen and increase of carbonic acid in the blood (Schwartz). This change in the blood needs to take place locally only in the vessels of the medulla oblongata, in order to produce this effect; it occurs, for example, from arrest of the blood in these vessels (by ligature of the carotid arteries, Kussmaul and Tenner, Rosenthal, or by closure of the venous currents from the brain, Hermann and Escher), by which their blood becomes progressively poorer in oxygen and richer in carbonic acid" (Hermann, "Grundriss der Physiologie des Menschen," Berlin, 1870, S. 160).

"If the supply of blood be cut off from the medulla by ligature of the blood-vessels of the neck, dyspnoea is produced, though the operation produces no change in the blood generally, but simply affects the respiratory condition of the medulla itself, by cutting off its blood-supply, the immediate result of which is an accumulation of carbonic acid and a paucity of available oxygen in the protoplasm of the nerve-cells in that region" (Foster, "A Text-Book of Physiology," London, 1877, p. 254).

These quotations from Hermann and from Foster show clearly that their idea is that the sense of want of air is due to deficiency of oxygenated blood in the medulla oblongata, a view fully sustained by my own experiments. The observations of Kussmaul and Tenner, referred to by Hermann, were made with reference to the cause of the convulsions which so often occur after profuse and sudden hemorrhage. They are to be found in the elaborate memoir by Kussmaul and Tenner, "On the Nature and Origin of Epileptiform Convulsions caused by Profuse Bleeding," translated and published by the "New Sydenham Society," in 1859. Kussmaul and Tenner made a large number of experiments on rabbits and horses, in which they observed the effects of tying the great vessels given off from the arch of the aorta. They noted, after this operation, great difficulty in respiration and violent convulsions. They did not, however, abolish the respiratory movements of the animal by artificial respiration, thus abolishing, for the time, the respiratory sense, and then note the effects of ligature of these vessels. The experiments by Rosenthal,

which are referred to, are probably those contained in his work on "*Die Athembewegungen und ihre Beziehungen zum Nervus Vagus*," Berlin, 1862. In these experiments, as I have already stated, it is shown that the respiratory efforts of an animal can be abolished by forcing atmospheric air or oxygen in large quantities through the lungs; but that the sense of want of air is felt when, in place of oxygen, nitrogen or hydrogen is employed, by this means removing the possibility of an irritation from carbonic acid. These are essentially the same as the observations made by Pflüger, in 1868. Rosenthal states very distinctly that the sense of want of air is due to want of oxygen-carrying blood in the medulla oblongata; but he does not actually demonstrate the truth of this proposition by experiments. The statements by Hermann and by Foster are apparently based upon the experiments of Kussmaul and Tenner and of Rosenthal; but I must nevertheless claim that the experiments which I have made upon this subject, which will be detailed farther on, if they should be confirmed, afford the first positive proof that the respiratory sense may be excited by cutting off the arterial supply from the medulla. There is nothing which I can find in the experiments of Kussmaul and Tenner or of Rosenthal to actually show that the sense of want of air is not due to a want of oxygen in the general system.

In reflecting upon this subject during the last few months, it occurred to me that the question was capable of a positive solution by experiment. If it is possible to cut off the arterial supply to the head and medulla oblongata, leaving the rest of the circulation free, an animal should make respiratory efforts, even though air is supplied to the lungs, provided that the sense of want of air is due to a want of oxygenated blood in the medulla. On the other hand, if the sense of want of air is due to a want of oxygen in the general system, cutting off the arterial supply from the head and medulla would have no more effect than cutting off the supply of oxygen from any other equally extensive part of the system. In reducing this idea to the project of an actual experiment, I conceived the following: I proposed to tie the vessels of supply to the medulla oblongata (the vessels given off from the arch of the aorta) and note the effects; and then to tie the descending aorta

in the chest and note the effects, leaving the vessels coming from the arch of the aorta free. It seemed to me that if the respiratory sense is due to want of oxygen in the general system, tying the aorta in the chest would induce respiratory efforts as promptly as cutting off the arterial supply from the medulla. With the view of settling this question if possible, I made the following experiments, which so far as they go are definite and satisfactory in their results. I propose, however, to extend these experiments, and I publish them now simply as preliminary to further investigations into the subject:

EXPERIMENT I., September 30, 1877.—A medium-sized, full-grown dog was brought completely under the influence of ether. The trachea was then opened and connected with a bellows and artificial respiration was maintained. Over the valve of the bellows was placed a sponge, which was saturated with ether from time to time, so that the animal was kept completely anesthetized during the experiment. The air in the bellows was also changed from time to time by pushing up the valve with the fingers and forcing out the vitiated air. The chest and abdomen were then laid open by a continuous incision in the median line, and the ribs were bent backward and secured with a strong cord tied behind the back, so that the lungs and heart were fully exposed. The pericardium was then cut away, the great vessels near the heart were isolated and loose ligatures were thrown around the trunk of the innominate artery, the left subclavian artery, the descending vena cava, the descending portion of the aorta and the ascending vena cava.* In this way, I was prepared to constrict the several vessels at will.

When these preliminary steps had been completed, the animal being entirely under the influence of ether and artificial respiration being kept up efficiently, there were absolutely no respiratory efforts, and the diaphragm, which was exposed, was quiescent.

The artificial respiration was then arrested. In forty-five seconds the animal began to make violent respiratory efforts. Artificial respiration was then resumed and the respiratory efforts of the animal ceased. When the artificial respiration was arrested, I first noticed a movement of the corners of the mouth at regular intervals and then the mouth was widely opened and the diaphragm became strongly contracted, also at regular intervals. The time was taken at the first violent respiratory effort.

The animal being quiet and making no efforts at respiration, the innominate artery, the left subclavian artery and the descend-

* In the dog the aorta gives off the innominate artery "which gives off first the left carotid, and then divides into the right subclavian and right carotid" (Foster, "Elementary Practical Physiology," London, 1876, p. 13). The left subclavian artery arises directly from the aorta.

ing vena cava were tied almost simultaneously, artificial respiration being constantly and efficiently maintained. In two minutes and eight seconds the animal began to make respiratory efforts, which continued so long as the vessels remained constricted.

The ligatures surrounding the vessels mentioned above were loosened five minutes and twenty-two seconds after they had been tied, and the respiratory efforts of the animal instantly ceased. After three minutes, artificial respiration was stopped, and the animal began to make respiratory efforts in thirty-nine and a half seconds, which ceased so soon as artificial respiration was resumed.

The descending aorta and the ascending vena cava in the chest were then tied simultaneously, the vessels arising from the arch of the aorta being free. This seemed to produce no effect, and no respiratory efforts were made by the animal for five minutes. The innominate artery and the left subclavian artery were then constricted, the aorta and ascending vena cava remaining tied. Respiratory efforts by the animal began in one minute and twenty-six seconds, although artificial respiration was maintained. These efforts ceased when the ligatures around the innominate and subclavian were loosened.

The ligatures were then removed from the descending aorta and ascending vena cava, and the innominate and left subclavian arteries were constricted, which was followed by respiratory efforts after one minute and six seconds. These efforts ceased when the vessels were freed.

The innominate artery alone was then constricted, but this seemed to produce no effect, no respiratory efforts being made by the animal for five minutes. At the end of five minutes the left subclavian artery was constricted, the constriction of the innominate artery being maintained. The animal began to make respiratory efforts fifty-three seconds after constriction of the subclavian. These efforts ceased on loosening the ligatures.

Artificial respiration was then stopped and the animal began to make respiratory efforts in ten seconds. The medulla oblongata was then broken up and the experiment was concluded.

In this experiment I had the aid of my assistant, Dr. C. F. Roberts, and of Mr. Gaspar Griswold, an advanced laboratory student. As the experiment progressed, it was ascertained that the vessels could be effectually constricted by making traction on the ligatures without tying. The constriction could then be instantly removed. It was also ascertained that constriction of the veins made no difference in the phenomena observed.

EXPERIMENT II., October 2, 1877.—A medium-sized, full-grown dog was brought completely under the influence of ether. A bellows was fixed in the trachea and the chest and abdomen were opened as in the preceding experiment. These preliminary steps were completed at 11.30 A. M. Artificial respiration, which had been kept up with the bellows, was arrested and the animal made efforts at respiration in thirty-seven and three-fifths seconds, having previously been quiet. The innominate artery and the left subcla-

vian artery were then constricted, the artificial respiration being continued, and the animal made respiratory efforts in two minutes and five seconds, having previously been rendered quiet by artificial respiration. After a few respiratory efforts the ligatures were loosened and the animal became perfectly quiet, artificial respiration being continued. While the animal was perfectly quiet, artificial respiration being continued, the descending aorta was tied in the chest. The aorta was constricted for five minutes and no effect was observed, artificial respiration being maintained and the animal remaining perfectly quiet. The heart was then cut out, the system being thus drained of blood, and the animal made respiratory efforts in twenty-five seconds.

This experiment was a public demonstration made in a lecture before the class at the Bellevue Hospital Medical College; and I was assisted by Dr. C. F. Roberts, Mr. Gaspar Griswold, Dr. G. S. Conant and Mr. W. L. Wardwell. The experiment was essentially a repetition of Experiment I., and the results of the two observations were nearly identical.

The two experiments just detailed show that ligature of the aorta has no sensible effect upon respiration; but that ligature of all the vessels given off from the arch of the aorta, which it would seem must cut off most of the supply of oxygenated blood from the brain and the medulla oblongata, produces a sense of want of air, which gives rise to respiratory efforts, even while artificial respiration is efficiently maintained. It seems, from the results observed in Experiment I., that it is not enough to tie the innominate artery, which is equivalent to tying the two common carotids and the right subclavian artery, but that it is necessary to tie also the left subclavian artery. This is explained by the fact that the left subclavian gives off the vertebral artery, which empties into the basilar artery and thus carries oxygenated blood to the medulla oblongata.

Taking into account the fact that the respiratory nerve-centre is situated in the medulla oblongata, the two experiments that I have described, so far as they go, seem to show conclusively that the sense of want of air is due to a deficiency of oxygenated blood in the medulla oblongata, and that this sense is satisfied by the circulation of such blood in the respiratory nerve-centre.

EXPERIMENT III., October 7, 1877.—A full-grown young dog, weighing about thirty pounds, was brought completely under the influence of ether at 10.45 A. M., a bellows was fixed in the trachea, and the chest and abdomen were opened as in the preceding ex-

periments. The vessels given off from the arch of the aorta were then carefully dissected out, and loose ligatures were thrown around the innominate artery, the two carotids, the right subclavian artery, the right vertebral artery, the left subclavian artery and the left vertebral artery. These ligatures were placed around the vessels so that they might be readily found in the course of the experiment, but the vessels were not thereby constricted.

After these preparatory steps had been completed, artificial respiration was arrested and the animal began to make respiratory efforts in thirty seconds. Artificial respiration was then resumed and the animal became quiet.

The two subclavian arteries were then constricted with *serrefines*, which, it was ascertained, arrested the blood-current completely. The animal remained quiet for five minutes, making no respiratory efforts. The subclavians remaining constricted, both carotids were then constricted in addition. The animal made respiratory efforts in two minutes and seven seconds after constriction of the carotids. All the vessels were then freed and the animal became quiet.

Both vertebral arteries and both carotids were then constricted for five minutes, the animal remaining quiet. These vessels remaining constricted, both subclavian arteries were constricted in addition. The animal made respiratory efforts in one minute and thirty-five seconds. All the vessels were then freed, and the animal became quiet.

At 11.40 o'clock the descending aorta in the chest and both subclavian arteries were tied. This left little more than the carotids to carry blood to the head, and the arterial blood was thus cut off from the greatest part of the system. The animal remained quiet for five minutes. The experiment had now lasted fifty-five minutes and the action of the heart had become considerably weakened. While the aorta and subclavians were still constricted, both carotids were constricted in addition. The animal remained quiet for five minutes, but the heart and the great vessels up to the points of constriction were enormously distended. At the end of this time the aorta was freed, which relieved the distension. The animal made respiratory efforts in two minutes and twenty-nine seconds, but the efforts were not very violent and were not so rapid as usual. All the vessels were freed and the animal became quiet.

Artificial respiration was then arrested and the animal made respiratory efforts in twelve seconds. Artificial respiration was resumed and the animal became quiet.

The innominate artery and the left subclavian artery were then constricted and the animal made respiratory efforts in one minute and fifteen seconds, but the action of the heart had become very feeble.

The experiment had lasted one hour and fifteen minutes and was concluded with the last observation.

In this experiment I was assisted by Dr. C. F. Roberts, Mr. Gaspar Griswold and Dr. G. S. Conant.

This experiment substantially confirmed the results obtained in Experiments I. and II. When the aorta, both subclavian arteries and both carotids were constricted, the pressure of blood in these vessels was enormous, and some blood may have found its way to the brain and medulla oblongata. The distension of the vessels was so great that this part of the experiment was not very satisfactory. Respiratory efforts were made by the animal, however, when the distension was relieved by freeing the aorta, the subclavians and the carotids remaining constricted.

In all the experiments the animals were kept completely under the influence of ether, and artificial respiration was kept up efficiently unless otherwise stated.

DEDUCTIONS AND CONCLUSIONS.—When I made my first experiments on the seat of the sense of want of air which gives rise to respiratory movements, in 1861, I attached to them considerable importance; and I thought that I had proved experimentally that the sense of want of air is due to a deficiency in oxygen in the system at large. The main features of the experiments which I made at that time I have already stated. My object in making these new experiments was to study the effects of cutting off the supply of oxygenated blood from different parts.

I think it may be assumed, as I have already stated, that the sole respiratory nerve-centre is in the medulla oblongata; and I endeavored to devise some means of cutting off the arterial supply of blood from this part. Animals respire when all of the encephalic centres have been destroyed except the medulla oblongata, so that it is improbable that cutting off the supply of blood from the brain would affect the muscles of respiration, provided artificial respiration is efficiently maintained. Blood can get to the medulla oblongata from the internal carotids, which are connected with the circle of Willis, from the vertebral arteries, which unite to form the basilar artery,* and perhaps from other vessels; but it is certain that if all the arteries given off from the arch of the aorta are tied the medulla must be deprived of oxygenated blood.

In Experiment I. the innominate artery and the left

* The basilar artery is much longer in the dog than in the human subject.

subclavian artery were constricted * and the animal made respiratory efforts in two minutes and eight seconds, notwithstanding that artificial respiration was kept up.

In Experiment II. the same vessels were constricted and the animal made respiratory efforts in two minutes and five seconds.

In Experiment III. both subclavian arteries and both carotids were constricted and the animal made respiratory efforts in two minutes and seven seconds. Both vertebral arteries and both carotids were constricted and the animal made no respiratory efforts for five minutes; but respiratory efforts were made in one minute and thirty-five seconds after both subclavians had been constricted in addition to the vertebrals and carotids.

It seems from all of these experiments that in order to induce respiratory efforts in an animal under the influence of ether and with the lungs supplied with air by artificial respiration, either the innominate artery and the left subclavian artery or both subclavians, both carotids and both vertebral arteries must be tied. In other words, according to my view of the cause of these respiratory efforts, the supply of blood to the medulla oblongata can not be cut off completely except by tying all the vessels given off from the arch of the aorta.

As the result of the experiments which I have just detailed, I must now modify the view which I advanced in 1861 as a conclusion from experiments then published, which I have maintained up to the present time, that the sense of want of air, which is the starting-point of the movements of respiration, is due to want of oxygen in the general system. My experiments made in 1861 were accurate and the conclusions from them seemed to be legitimate; but these experiments were incomplete. The experiments which I have just reported, taken in connection with my experiments of 1861, lead me to conclude that the sense of want of air is due to a want of circulation of oxygenated blood in the medulla oblongata.

I trust that my experiments, which are by no means difficult or uncertain in their results, may be repeated and

* In the first experiment the great veins were also tied, but this seemed to make no difference in the phenomena following constriction of the arteries, and the veins were left free in the other experiments.

either verified or corrected by other physiologists. The idea that the sense of want of air is due to a deficiency of oxygen in the medulla has been adopted by some writers; but so far as I know, my experiments are the first to show, by actual demonstration, that this view is correct.

In another paper I propose to treat of the respiratory sense much more fully and to review the literature of the subject. Many interesting and important points will undoubtedly be involved in a full discussion of the nervous mechanism of the respiratory movements; and among them will be the question as to whether the normal respiratory movements are actually reflex in their character, as has been generally supposed, or whether they are due to a direct excitation of the nerve-cells in the respiratory centre.

VIII

IS THE ACTION OF THE MEDULLA OBLONGATA IN NORMAL RESPIRATION REFLEX?

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IN connection with a series of experiments published in 1877, the question occurred to me whether or not the action of the medulla oblongata in normal respiration could strictly be classed among those operations recognized by physiologists as reflex. That the medulla oblongata contains the centre presiding over certain reflex phenomena, acting through some special nerves, there can be no doubt. The centres in the medulla seem to serve as coördinators of the muscles of expression, and have certain reflex functions connected with the respiratory muscles, such as coughing, sneezing, etc. In certain instances, also, in which respiration is temporarily suspended, a stimulation of parts of the general surface, as by a dash of cold water, will excite respiratory movements. Such an action as the one last mentioned might properly be called reflex; but the phenomena which I here propose to consider are those of ordinary, normal respiration and the exaggerations of the respiratory sense which amount to a more or less intense feeling of want of air.

The general view under which physiologists have been accustomed to regard the respiratory movements as reflex is the following: It has been thought that there existed in some part of the organism or in the system at large a certain sense, which may be called the sense of want of air, the respiratory sense, or the "besoin de respirer," of the French, dependent upon either an actual or an impending deficiency of oxygen or upon an impression produced by the circulation of blood containing carbonic acid in parts that should normally receive oxygenated blood. This "respiratory sense" has been taken as the starting-

point of the respiratory acts. Regarding a reflex phenomenon as involving an impression conveyed by afferent nerves to a nerve-centre, which impression, by the action of the nerve-centre, is converted into a stimulus and is reflected along certain efferent nerves to muscles, the conditions of the operation of reflex action in ordinary respiration have been regarded as complete. The respiratory sense, according to this view, is conveyed by certain centripetal nerves to the medulla oblongata, and here it is converted into a stimulus which is conveyed by the proper centrifugal nerves to the respiratory muscles, and there follows an act of inspiration.

My principal object, in this article, is to discuss the question of the so-called reflex action of the medulla oblongata in respiration, drawing conclusions mainly from my own experiments. I shall not, therefore, attempt to give a full account of the literature bearing upon the action of the medulla oblongata as the respiratory nerve-centre or even of the experiments which relate to its reflex function, except in so far as the latter have been followed by important advances or changes in the views of physiologists or as their history involves questions of priority.

In 1809 Legallois made a number of experiments upon rabbits in which he showed that respiration ceased suddenly when a section of the medulla oblongata was made to include the origin of the eighth pair of nerves; but that the respiratory acts continued when the cerebrum, cerebellum and a part of the medulla oblongata were removed by successive slices from before backward.* Flourens extended the observations of Legallois and fixed the limits of the respiratory nerve-centre in the rabbit, between the upper border of the origin of the pneumogastrics and a line drawn about a quarter of an inch below the lowest point of origin of these nerves.† Longet and Flourens, in later observations, restricted the limit still further, and showed that it was confined to the gray matter of the lateral tracts, or the intermediary fasciculi.‡ Since the publi-

* Legallois, "Expériences sur le principe de la vie." Œuvres, Paris, 1824, tome i., p. 64. The date of these experiments is given by Legallois on page 71 of the above-mentioned work.

† Flourens, "Système nerveux," Paris, 1842, p. 204.

‡ Longet, "Traité de physiologie," Paris, 1869, tome iii., pp. 387, 388.

cation of the experiments of Flourens, nearly all physiologists have agreed that the respiratory nerve-centre is situated in some part of the gray matter of the medulla, and this view I accept without reserve. Its most notable opponent, however, is Dr. Brown-Séquard. This author contends that the arrest of respiratory movements which follows destruction of the medulla is due to irritation of surrounding parts and not to the destruction of the so-called respiratory centre; and that in certain cases, the movements may become reestablished after the irritation has subsided.* In the absence of their full confirmation by other observers, I do not regard the experiments or the conclusions of Dr. Brown-Séquard as satisfactory; and I still hold that the medulla oblongata is the centre presiding over the respiratory acts.

Marshall Hall, in his memoir on the "Reflex Function of the Medulla Oblongata and Medulla Spinalis," published in 1833, says nothing in regard to the reflex character of respiration. In the Croonian Lectures, delivered before the Royal College of Physicians in 1850, he advances the view that the normal respiratory acts are reflex and dependent upon excitation of the pneumogastric nerves by the accumulation of carbonic acid evolved in the lungs from the venous blood.† Subsequent observations, however, have shown that the theory proposed by Marshall Hall is incorrect; and at the present day it is not adopted by any physiologist of recognized authority. As early as 1839, John Reid suggested that the sense of want of air was due in a measure to the circulation of venous blood in the medulla oblongata.‡ This fact is interesting in view of the results of recent experiments which will be detailed farther on. In 1841 Volkmann made a number of experiments, the conclusion drawn from which was that the sense of want of air depends upon a certain condition of the general

* Brown-Séquard, "Recherches sur les causes de mort après l'ablation de la partie de la moelle allongée qui a été nommée point vital." *Journal de la physiologie*, Paris, 1858, tome i., p. 217 *et seq.*; and "Recherches expérimentales sur la physiologie de la moelle allongée." *Ibid.*, 1860, tome iii., p. 151 *et seq.*

† Marshall Hall, "Synopsis of the Diastaltic Nervous System," London (no date), p. 43.

‡ Reid, "An Experimental Investigation into the Functions of the Eighth Pair of Nerves," etc., Part Second. "Anatomical and Physiological Researches," Edinburgh, 1848, p. 285; and "Edinburgh Medical and Surgical Journal," April, 1839.

system as well as an impression made upon the pulmonary mucous membrane.

"The respiratory movements appear really to be of a reflex character in the following way: The exciting agent is carbonic acid—not that which has become free in the air passages, but that which is contained in the blood; the situation of the stimulation is in every part of the body, not alone the pulmonary mucous membrane; finally, the nerves brought into action are all nerves which conduct centripetally operating toward the medulla oblongata, not exclusively the vagus."*

Volkman states, immediately following the passage just quoted, that the respiratory movements find their impulse in a "respiratory necessity"; and that this originates in the entire system; that all animals require oxygen from the blood in place of the carbonic acid which they give up to the blood; and that so soon as the blood is overcharged with carbonic acid, this "necessity" (respiratory) can not be satisfied.

In 1861 I made a series of experiments with the view of ascertaining the situation of the respiratory sense, adopting the view, which was then almost universally received, that the respiratory acts are reflex.† The main points in these experiments were the following:

When the chest was opened in a living dog and a bellows fixed in the trachea, so long as artificial respiration was efficiently performed the animal made no respiratory efforts. In these experiments the animals usually were etherized; but in several instances they were allowed to come from under the influence of the anesthetic. The diaphragm and other important respiratory muscles were denuded and fully exposed to view. This was almost an exact repetition of an experiment performed by Robert Hooke in 1664.

An artery was then opened and the blood was allowed to flow in a small stream. When the artificial respiration was suspended the animal began to make respiratory efforts so soon as the blood became dark in the arteries; but

* Volkman, "Ueber die Bewegungen des Athems und Schluckens," etc. "Archiv für Anatomie, Physiologie, und wissenschaftliche Medicin," Berlin, 1841, S. 342.

† Flint, "Experimental Researches on Points connected with the Action of the Heart and with Respiration."—"American Journal of the Medical Sciences," October, 1861, p. 372 *et seq.*

when artificial respiration was resumed, so soon as the blood became again bright red in the arteries the respiratory efforts ceased.

In order to ascertain whether the sense of want of air was due to a deficiency of oxygen or to the presence of carbonic acid in the blood of the arteries, I drained the animals of blood, sometimes from a large artery and sometimes by excising the heart, at the same time keeping up artificial respiration carefully and efficiently. As the system became drained of blood, there always occurred vigorous and even violent respiratory efforts, although the lungs were kept supplied with pure air.

From these experiments I reasoned that the respiratory movements being, as I thought, reflex, the sense of want of air depended upon a deficiency of oxygen in the system at large and not upon the presence of carbonic acid in the blood of the arteries; for the sense seemed to be felt by the animals in my experiments, when the system was drained of blood, the arteries containing no blood charged with carbonic acid.

In 1868, about seven years after the publication of my experiments in the "American Journal of the Medical Sciences," Pflüger published a very interesting article upon the same question.* In this article a very elaborate review is given of the literature of the subject. He first refers to the opinions of various authors in regard to the question of a difference in color between the blood of the umbilical arteries and the umbilical vein, and then goes on to state that "it is established without doubt that, after birth, there is a diminution in the quantity of oxygen in the body of the newly born, which, as the following researches will show, is the real cause of respiration." The experiments which led Pflüger to the conclusion that the sense of want of air, dyspnoea, and apnoea were due to a want of oxygen in the system consisted mainly in causing animals to breathe an irrespirable gas, such as pure nitrogen.†

* Pflüger, "Ueber die Ursache der Athembewegungen, sowie der Dyspnoë und Apnoë."—"Archiv für die gesammte Physiologie," Bonn, 1868, Bd. i., S. 61 *et seq.*

† Rosenthal, in his work on the "Respiratory Movements," published in 1862, anticipated the experiments of Pflüger upon the influence of the insufflation of irrespirable gases upon the respiratory movements. He noted that the manifestations of dyspnoea ceased in animals when the chest had been opened

"Using blood-letting for ascertaining the condition of the blood during dyspnœa, I arrived at the following facts: As soon as the dog begins to breathe pure nitrogen, it is scarcely fifteen seconds before he makes violent and deep inspirations; at the end of thirty seconds, the most intense dyspnœa is observed, the blood is already almost absolutely black, which must be due to the enormously rapid tissue-metamorphosis of the animal. At the end of one minute the animal is already almost asphyxiated. The respiratory movements are very infrequent or have ceased, but the heart still beats." *

Then follows a series of examinations of the blood under normal conditions at various times after causing an animal to breathe pure nitrogen. In one of these observations, after causing a dog to breathe nitrogen for one minute, the oxygen of the blood was found to be reduced from 14.35 per cent. to 0.2 per cent., and the carbonic acid from 36.9 per cent. to 29.9 per cent., showing a very great diminution in oxygen and a considerable diminution in carbonic acid. "No one, therefore, can be of the opinion that dyspnœa and asphyxia in breathing indifferent gases is connected with the accumulation of carbonic acid." †

While Pflüger assumed to give a review of the literature of the subject under investigation, he made no mention of my experiments published in 1861, although the results were nearly identical with his own. Later observations and experiments, however, have convinced me that the interpretations of my earlier experiments, as well as those made by Pflüger, were incorrect. I do not now believe that the acts of respiration are purely reflex in the sense in which this term is generally used; and I do not believe that the sense of want of air is due to a deficiency of oxygen in the system at large. I have become convinced, by experiments made in 1877, that the real cause of the sense of want of air, with its various exaggerations and modifications, is a deficiency in or an absence of oxygenated

and oxygen was passed through the lungs, but that they continued when, instead of oxygen, nitrogen or hydrogen was used, "although in this case the carbonic acid, as well as the oxygen, was removed from the blood." From this it appears to follow that it is not the increased quantity of carbonic acid, but the diminished quantity of oxygen which, in dyspnœa, produces the mediate or the immediate stimulation of the respiratory central organ. (Rosenthal, "Die Athembewegungen," etc., Berlin, 1862, S. 4.) My own experiments were published in 1861.

* Pflüger, *op. cit.*, S. 89.

† Ibid., S. 95.

blood in the vessels of the medulla oblongata. This opinion has been entertained by certain physiologists on theoretical grounds; but so far as I know, it had not been sustained by direct experiment prior to my observations in 1877.

In 1877 I made a series of experiments which seemed to me to demonstrate conclusively that the sense of want of air is due to a deficiency of oxygen-carrying blood in the medulla oblongata. The details of these experiments have already been published,* and I shall here give merely a summary of the results.

If the chest of a dog is opened, the animal being under the influence of ether, and if artificial respiration is efficiently maintained the animal will make no respiratory efforts so long as fresh air in sufficient quantity is supplied to the lungs. This is an old experiment, dating from the time of Robert Hooke, in 1664, and has been repeatedly verified.

Air still being supplied in adequate quantity to the lungs, if the aorta is tied or the system drained of blood, the animal will make violent respiratory efforts under the influence of the sense of want of air. This is due to the fact that the oxygen can not get to the system or to some part or parts of the system; and this demonstration was made and published by me as early as 1861. Similar results were obtained by Rosenthal in 1862 and by Pflüger in 1868.

In 1877 it occurred to me that it was possible to ascertain by experiment whether the sense of want of air was due to a want of oxygen in the general system or in some restricted part. It being so well established that the medulla oblongata is the respiratory nerve-centre, I was naturally led to look for some means of cutting off the supply of blood from this part. This can easily be done by tying the innominate artery and the left subclavian artery in a dog, in this animal the aorta giving off from the arch these two vessels which are the only sources of supply of blood to the head and the anterior extremities. The following experiment, which I copy from my article published in 1877, shows the effect of constricting the vessels given off from the arch of the aorta. This experiment is a type

* Flint, "Experiments on the Effects upon Respiration of cutting off the Supply of Blood from the Brain and the Medulla Oblongata."—"New York Medical Journal," November, 1877, vol. xxvi., p. 449.

of many others made in my laboratory and in public demonstrations.

September 30, 1877.—A medium-sized, full-grown dog was brought completely under the influence of ether. The trachea was then opened and connected with a bellows and artificial respiration was maintained. Over the valve of the bellows was placed a sponge, which was saturated with ether from time to time, so that the animal was kept completely anesthetized during the experiment. The air in the bellows was also changed from time to time by pushing up the valve with the fingers and forcing out the vitiated air. The chest and abdomen were then laid open by a continuous incision in the median line, and the ribs were bent backward and secured with a strong cord tied behind the back, so that the lungs and heart were fully exposed. The pericardium was then cut away, the great vessels near the heart were isolated and loose ligatures were thrown around the trunk of the innominate artery, the left subclavian artery, the descending vena cava, the descending portion of the aorta, and the ascending vena cava.* In this way, I was prepared to constrict the several vessels at will.

When these preliminary steps had been completed, the animal being entirely under the influence of ether and artificial respiration being kept up efficiently, there were absolutely no respiratory efforts, and the diaphragm, which was exposed, was quiescent.

The artificial respiration was then arrested. In forty-five seconds the animal began to make violent respiratory efforts. Artificial respiration was then resumed, and the respiratory efforts of the animal ceased. When the artificial respiration was arrested, I first noticed a movement of the corners of the mouth at regular intervals and then the mouth was widely opened and the diaphragm became strongly contracted, also at regular intervals. The time was taken at the first violent respiratory effort.

The animal being quiet and making no efforts at respiration, the innominate artery, the left subclavian artery and the descending vena cava were tied almost simultaneously, artificial respiration being constantly and efficiently maintained. In two minutes and eight seconds the animal began to make respiratory efforts, which continued so long as the vessels remained constricted.

The ligatures surrounding the vessels mentioned above were loosened five minutes and twenty-two seconds after they had been tied, and the respiratory efforts of the animal instantly ceased. After three minutes, artificial respiration was stopped, and the animal began to make respiratory efforts in thirty-nine and a half seconds, which ceased so soon as artificial respiration was resumed.

The descending aorta and the ascending vena cava in the chest

* In the dog, the aorta gives off the innominate artery, "which gives off first the left carotid, and then divides into the right subclavian and right carotid" (Foster, "Elementary Practical Physiology," London, 1876, p. 13). The left subclavian artery arises directly from the aorta.

were then tied simultaneously, the vessels arising from the arch of the aorta being free. This seemed to produce no effect, and no respiratory efforts were made by the animal for five minutes. The innominate artery and the left subclavian artery were then constricted, the aorta and ascending vena cava remaining tied. Respiratory efforts by the animal began in one minute and twenty-six seconds, although artificial respiration was maintained. These efforts ceased when the ligatures around the innominate and subclavian were loosened.

The ligatures were then removed from the descending aorta and ascending vena cava, and the innominate and left subclavian arteries were constricted, which was followed by respiratory efforts after one minute and six seconds. These efforts ceased when the vessels were freed.

The innominate artery alone was then constricted, but this seemed to produce no effect, no respiratory efforts being made by the animal for five minutes. At the end of five minutes the left subclavian artery was constricted, the constriction of the innominate artery being maintained. The animal began to make respiratory efforts fifty-three seconds after constriction of the subclavian. These efforts ceased on loosening the ligatures.

Artificial respiration was then stopped and the animal began to make respiratory efforts in ten seconds. The medulla oblongata was then broken up and the experiment was concluded.

In this experiment I had the aid of my assistant, Dr. C. F. Roberts, and Mr. Gaspar Griswold, an advanced laboratory student. As the experiment progressed, it was ascertained that the vessels could be effectually constricted by making traction on the ligatures without tying. The constriction could then be instantly removed. It was also ascertained that constriction of the veins made no difference in the phenomena observed.

The general result of all my experiments made on the plan of the one just detailed was that invariably, when the innominate and the left subclavian artery were tied, the dogs began to make respiratory efforts in a little more than two minutes after the ligation, but the animals remained quiet after ligation of the aorta in the chest. The respiratory efforts continued so long as the vessels going off from the arch of the aorta remained constricted, and they ceased almost immediately when the ligatures were loosened. During all of my observations upon the effects of tying the various bloodvessels, artificial respiration was kept up constantly and efficiently. Under the view which I was led to adopt by the results of these experiments—that the sense of want of air was due to a deficiency of oxygen-carrying blood in the medulla oblongata—I could not be certain that the arterial blood was entirely shut off

from the medulla without tying the innominate and the left subclavian. It seemed to make no difference in the results of the experiments whether the great veins were tied or left free. In all of the experiments the excitability of the medulla was repeatedly shown by arresting artificial respiration from time to time. The animals began to make respiratory efforts in thirty to forty-five seconds after the arrest of artificial respiration.

The results of my experiments show that when the flow of oxygenated blood is cut off from the parts supplied by the vessels given off from the arch of the aorta in a living animal, the sense of the want of air is excited, as is evident from repeated and often violent respiratory efforts, although air is supplied to the lungs. Respiration will continue when all of the encephalic ganglia, with the exception of the medulla oblongata, have been removed; and it is well known that this, the medulla, is the sole respiratory nervous centre. One would naturally look, then, to influences operating upon the medulla oblongata for an explanation of these respiratory efforts. It does not seem that these movements can be due to an impression received by the medulla from the general system and due to want of oxygen; for when the descending aorta is tied in the chest no respiratory efforts are made. The movements, indeed, occur only when the medulla oblongata is deprived of blood; and the vessels which it is necessary to tie in order to produce this result involve a smaller part of the general systemic circulation than when the descending aorta is tied in the chest.

I do not assume that the view just enunciated is entirely novel; but so far as I know, the observations made in 1877 were the first to sustain such a view by positive experimental evidence. Upon this point I have nothing to add to what I have already stated in connection with the following quotations: *

"The first respiratory effort of the fœtus is thus produced by the interruption of the placental respiration, the sudden deficiency of oxygen and increase of carbonic acid in the blood (Schwartz). This change in the blood needs to take place locally only in the vessels of the medulla oblongata, in order to produce this effect; it occurs, for example, from arrest of the blood in these vessels

* "New York Medical Journal," November, 1877, vol. xxvi., p. 452.

(by ligature of the carotid arteries, Kussmaul and Tenner, Rosenthal, or by closure of the venous currents from the brain, Hermann and Escher), by which their blood becomes progressively poorer in oxygen and richer in carbonic acid" (Hermann, "Grundriss der Physiologie des Menschen," Berlin, 1870, S. 160).

"If the supply of blood be cut off from the medulla by ligature of the blood-vessels of the neck, dyspnoea is produced, though the operation produces no change in the blood generally, but simply affects the respiratory condition of the medulla itself, by cutting off its blood supply, the immediate result of which is an accumulation of carbonic acid and a paucity of available oxygen in the protoplasm of the nerve-cells in that region." (Foster, "A Text-Book of Physiology," New York, 1880, p. 377.)

These quotations from Hermann and from Foster show clearly that their idea is that the sense of want of air is due to deficiency of oxygenated blood in the medulla oblongata, a view fully sustained by my own experiments. The observations of Kussmaul and Tenner, referred to by Hermann, were made with reference to the cause of the convulsions which so often occur after profuse and sudden hemorrhage. They are to be found in the elaborate memoir by Kussmaul and Tenner, "On the Nature and Origin of Epileptiform Convulsions caused by Profuse Bleeding," translated and published by the "New Sydenham Society," in 1859. Kussmaul and Tenner made a large number of experiments on rabbits and horses, in which they observed the effects of tying the great vessels given off from the arch of the aorta. They noted, after this operation, great difficulty in respiration and violent convulsions. They did not, however, arrest the respiratory movements of the animal by artificial respiration, thus abolishing, for the time, the respiratory sense, and then note the effects of ligature of these vessels. The experiments by Rosenthal, which are referred to, are probably those contained in his work "Die Athembewegungen und ihre Beziehungen zum Nervus Vagus," Berlin, 1862. In these experiments, as I have already stated, it is shown that the respiratory efforts of an animal can be abolished by forcing atmospheric air or oxygen in large quantities through the lungs, but that the sense of want of air is felt when, in place of oxygen, nitrogen or hydrogen is employed, by this means removing the possibility of an irritation from carbonic acid. These are essentially the same as the observations made by Pflüger, in 1868. Rosenthal states very distinctly that the sense of want of air is due to want of oxygen-carrying blood in the medulla oblongata; but he does not actually demonstrate the truth of this proposition by experiments. The statements by Hermann and Foster are apparently based upon the experiments of Kussmaul and Tenner and of Rosenthal; but I must nevertheless claim that the experiments which I have made upon this subject, which will be detailed farther on, if they should be confirmed, afford the first positive proof that the respiratory sense may be excited by cutting off the arterial supply from the medulla. There is nothing which I can find, in the experiments of Kussmaul and Tenner or of Rosenthal, which actually shows

that the sense of want of air is not due to a want of oxygen in the general system.

All the experiments that I have thus far referred to have of necessity involved placing the animals on which the observations were made under conditions exceedingly unnatural. It can not be assumed that after the chest has been opened the nerve-centres possess a degree of sensibility and a power of action entirely normal. Still it is not easy to see how such a modification of the natural conditions can be avoided; and we must reason as best we can from the observations that have been made, keeping in view the experimental conditions.

It is certain that oxygen may be artificially supplied to the lungs in a living animal so efficiently as to abolish for the time the sense of want of fresh air, to satisfy the requirements of the system for oxygen and to cause all respiratory efforts on the part of the animal to cease. When artificial respiration is arrested and the blood becomes dark in the arteries, when the blood is drained from the system, artificial respiration being continued, or when oxygenated blood is shut off from the medulla oblongata, the animal makes respiratory efforts.

Taking into consideration all the experiments bearing upon this point, they seem to show beyond question that, under the conditions indicated above, the sense of want of air, the stimulus or whatever it may be that causes the animal to make respiratory efforts depends upon some peculiar condition in the medulla oblongata. Still, under the conditions mentioned; that is, an animal under the influence of ether with the chest opened and a bellows in the trachea, when artificial respiration is interrupted, the respiratory efforts begin in thirty to forty-five seconds. There is then blood in the medulla oblongata, containing less oxygen and more carbonic acid than normal arterial blood and passing through the capillaries under great pressure, slowly and with difficulty. When, on the other hand, all the vessels given off from the arch of the aorta are tied, respiratory efforts begin in a few seconds more than two minutes. While this latter experiment, taken by itself, shows that shutting off the oxygen-carrying fluid from the medulla oblongata excites the sense of want of air, the question at once arises: why, when the vessels

which supply the medulla oblongata are filled with blood of a venous character, is the respiratory sense excited so much more promptly than when the arteries are tied? In other words, if it is assumed that shutting off the blood from the medulla oblongata will excite the respiratory sense by cutting off the supply of oxygen, and that this will induce respiratory efforts in about two minutes, why does the simple interruption of artificial respiration, which causes blood of a venous character to go to the medulla oblongata, induce respiratory efforts in about thirty seconds?

This is a question which I have in vain attempted to solve to my entire satisfaction. When artificial respiration is arrested and the circulation is not interfered with by the tying of vessels, the venous blood passes through the lungs and back to the left side of the heart without losing its carbonic acid and without receiving a fresh supply of oxygen. Under these conditions, it passes through the great vessels given off from the arch of the aorta to the medulla oblongata as well as to other parts; and the main obstruction to the blood-current, which produces such intense engorgement of the cardiac cavities, exists in the systemic capillaries. It is fair to infer that the capillaries of the medulla are engorged as well as others. This being the condition, it is logical to assume that the oxidizing processes which normally go on in the medulla are promptly arrested; and it may also be assumed, for sake of argument, that this arrest of oxidation excites the sense of want of air. It does not appear how any experiment can be devised in which the venous blood could be admitted in such quantity to the medulla, at the same time maintaining the normal supply of oxygen and the uninterrupted performance of normal oxidation in this particular part.

On the other hand, suppose that the great vessels given off from the arch of the aorta are tied! While the supply of fresh arterial blood is thus cut off from the medulla, it is well known that the contraction of the vessels beyond the point of ligation, which is slow and gradual, as is characteristic of non-striated muscular tissue, will still force the small quantity of blood which these vessels contain through the medulla. My experiments show that the supply of arterial blood to the medulla need not be very con-

siderable in order to satisfy the respiratory sense. Constriction of the innominate artery alone does not induce respiratory efforts. No respiratory efforts are made when both carotids and both vertebral arteries are constricted. These efforts, indeed, occur only when the innominate and the left subclavian are tied, or when ligatures are applied to both carotids, both vertebrals and both subclavians.

Reasoning from these facts and inferences, the following is the only explanation that I can offer of the rapid excitation of respiratory efforts by simple arrest of artificial respiration, as compared with the effects of tying the vessels given off from the arch of the aorta:

When artificial respiration is interrupted, the normal oxidizing process in the medulla oblongata is promptly arrested and respiratory efforts begin in thirty to forty-five seconds. When, on the other hand, the vessels which supply blood to the medulla are tied, the contraction of the muscular coats of the vessels beyond the points of ligation for a certain time forces a small quantity of arterial blood to the medulla, and it is only when this ceases that the want of oxygen is felt. This may be the reason why the arrest of oxidation in the medulla is later when the vessels are tied than when artificial respiration is interrupted.

When it is proved, as I think it has been proved conclusively, that an animal, after the respiratory movements have been arrested by artificial respiration, will make respiratory efforts when the supply of oxygen-carrying blood is shut off from the medulla oblongata, the question arises in regard to the application of this experimental fact to the mechanism of normal respiration.

CAUSE OF THE NORMAL RHYTHMICAL MOVEMENTS OF RESPIRATION.—The normal rhythmical movements of respiration are excited and regulated by the respiratory nerve-centre in the medulla oblongata. Under ordinary physiological conditions the exciting cause of these movements, whatever it may be, is unconscious; and the muscular acts by which air is introduced into the lungs take place without efforts of the will. In other words, the movements of ordinary respiration are unconscious and involuntary. That these propositions are correct has been proved by experiments that are perfectly familiar to physiologists.

When all the nerve-centres that are known to have any relations to sensation and voluntary movements are destroyed, the medulla oblongata remaining intact, the rhythmical movements of respiration persist. When the medulla oblongata is destroyed, the other nerve-centres remaining intact, the respiratory movements are instantly arrested. The cause of this arrest of respiratory movements following destruction of the medulla is explained by the following proposition:

The medulla oblongata contains the only nerve-centre capable of appreciating the unconscious sense of want of air; and consequently, when this centre is destroyed, the sense of want of air is not felt and no true respiratory movements can be excited. In the same way, when oxygen is freely supplied to the blood of a living animal by artificial means, no sense of want of air exists and no respiratory efforts occur. In the fœtus in utero, so long as oxygen is supplied to the blood by the placenta, no respiratory efforts are made; but when the placental circulation is interrupted, the sense of want of air is developed and respiratory efforts occur. This may take place, as is well known, before birth.

My experiments published in 1877 show conclusively that the sense of want of air is developed and respiratory efforts are excited, not necessarily by a possible irritation due to the circulation of venous blood in the medulla oblongata, but by cutting off from the medulla the supply of oxygen. This occurs when the respiratory acts have been arrested by supplying air to the lungs artificially.

Under ordinary physiological conditions, the heart-beats numbering seventy-two and the respirations eighteen per minute, the following is probably the mechanism of the flow of blood through the capillaries of the lungs and the vessels of the medulla oblongata:

The venous blood from the general system is sent to the lungs by the action of the right ventricle, the intermittent force of which is absorbed by the elasticity of the pulmonary artery and its branches, until the current in the pulmonary capillaries becomes nearly or quite steady and continuous. This venous blood is poor or deficient in oxygen and rich in carbonic acid. As it passes through the lungs it gives off its carbonic acid and takes up oxygen.

In the pulmonary vesicles the composition of the air is tolerably uniform; that is, it contains a certain proportion of oxygen and of carbonic acid. But at the same time, the air in the pulmonary cells has a tendency to an increase in its proportion of carbonic acid with a diminution in its oxygen; for the venous blood, as it passes through the pulmonary capillaries, is constantly giving off carbonic acid and taking up oxygen. This tendency to a diminution in oxygen and an increase in carbonic acid in the contents of the air cells progressively increases from the completion of any single inspiratory act to the beginning of another. When, however, a new act of inspiration occurs, fresh oxygen is introduced into the lungs, which supplies the place of a certain quantity of carbonic acid thrown off by the preceding expiration. That this occurs is sufficiently evident; and it is illustrated by the fact that when expiration is voluntarily retarded, the expired air becomes richer in carbonic acid and poorer in oxygen than it is under ordinary conditions.

On the other hand, the left ventricle is sending arterial blood received from the lungs to all parts of the system, including the medulla oblongata. The elasticity of the aorta and of its branches gradually extinguishes or absorbs the intermittent force of the heart, so that the blood flows in a steady and continuous stream through the capillaries of the medulla. But as the tendency of the air in the pulmonary parenchyma is to progressively increase its proportionate quantity of carbonic acid and to diminish its oxygen between two inspiratory acts, the tendency of the blood coming from the lungs and sent by the left ventricle to the medulla oblongata is to become progressively poorer in oxygen. After about four revolutions of the heart (assuming that the proportion of the beats of the heart to the respiratory acts is as four to one), the quantity of oxygen supplied to the medulla oblongata has become so far diminished that there occurs an unconscious sense of want of air, and this excites a new inspiratory act. So it is, in all probability, that the normal, rhythmical acts of inspiration are periodically excited; and anything, like violent muscular exercise, that increases the activity of the consumption of oxygen, of necessity increases the number of respirations per minute.

In my opinion, in the explanation just given of the cause of the rhythmical acts of respiration, I have gone as far as I can, in the present condition of physiological knowledge, without becoming involved in unprofitable speculation and in a discussion of propositions not justified by established facts. All that can at present be positively assumed to be true, is that respiratory movements are excited by a want of oxygen in the substance of the medulla oblongata; and I know of no reasonable theory that will explain the exact mode of action of the oxygen of the blood upon any of the anatomical elements of the respiratory nerve-centre. Still it may not be uninteresting to refer to an explanation, proposed by Pflüger * in 1868 and advanced again in 1878 by Burkart, the substance of which is contained in the following quotation:

"1. The ganglionic cells of the respiratory centre produce, when there is a deficiency of oxygen, a readily oxidizable substance. 2. This substance performs its function, through a certain degree of production and accumulation, as a stimulus to the very cells that are concerned in its production. 3. The oxygen of the blood, that is of the tissues, operates against the production and accumulation, and consequently the stimulating action of this hypothetical substance thus restrained or removed. The capacity of the ganglionic cells to produce, in a greater or less degree, by a deficiency of oxygen, this substance which excites respiratory movements, is measured by the vital energy of the cells, as far as this vital energy, or better the energy of the process of oxidation, relates to the demand for oxygen on the part of the cells. The production of the hypothetical substance is merely the vital expression of the ganglionic cells of the respiratory centre through a deficiency in oxygen, and it ceases with the life of the cells themselves." †

The above quotation, which it was somewhat difficult to render into idiomatic English, embodies a theory which may be more clearly expressed as follows:

The nerve-cells of the respiratory centre are constantly producing a hypothetical substance which acts as a stimulus to the muscles of inspiration. As the arterial blood passes through the capillaries of the medulla, its oxygen combines with this hypothetical substance, which is thus

* Pflüger, "Ueber die Ursache der Athembewegungen, sowie der Dyspnœ und Apnœ."—"Archiv für die gesammte Physiologie," Bonn, 1868, Bd. i., S. 90.

† Burkart, "Studien über die automatische Thätigkeit des Athemcentrums und über die Beziehungen desselben zum Nervus Vagus und anderen Athemnerven."—"Archiv für die gesammte Physiologie," Bonn, 1878, Bd. xvi., S. 436.

destroyed, or at least its action as a stimulus to the muscles of respiration is arrested. The quantity of this substance existing in the cells of the medulla is regulated by the supply of oxygen, and this regulates the degree of stimulation of the respiratory muscles. The production of this hypothetical substance is a manifestation of the vital energy of the cells, and this production ceases with the life of the cells.

The theory which I have proposed involves the following simple propositions, deduced mainly from my experiments published in 1877:

1. When the respiratory nerve-centre is fully supplied with oxygen by means of artificial respiration, this centre gives off no stimulus to the muscles of inspiration and no respiratory efforts occur.

2. When there is a deficiency in the supply of oxygen to the respiratory nerve-centre, the stimulus which gives rise to inspiratory efforts is generated; and this stimulus and the respiratory efforts which follow are active and vigorous in proportion to the extent and duration of the deficiency of oxygen.

3. In normal respiration, expiration being mainly passive, the rhythm and extent of the inspiratory acts are regulated by the quantity of oxygen supplied to the medulla oblongata. Thus, when there is a tendency to a deficiency of oxygen in the arterial blood, as its proportion must gradually and progressively diminish from the end of one inspiratory act to the beginning of another, this need of oxygen, or unconscious sense of want of air, induces a stimulus which leads to the introduction of fresh air into the lungs.

4. As oxygen can get to the medulla oblongata only through the blood, serious disturbances of the circulation are always attended with an exaggeration of the respiratory sense, although the lungs may be freely supplied with pure air.

The theory of Burkart involves the assumption of the existence of a "readily oxidizable substance" which the cells of the medulla oblongata have a constant tendency to produce and which the oxygen of the blood has a constant tendency to destroy. Burkart assumes that this hypothetical substance acts as a stimulus to the muscles of

inspiration; I contend that it is not logical to go farther in an explanation of the generation of the respiratory stimulus than to state the fact, which I have demonstrated experimentally, that the sense of want of air, be it unconscious, as in ordinary respiration, or conscious, as it is when it becomes a sense of suffocation, is due to a deficiency in the supply of oxygen to the respiratory nerve-centre.

CAUSE OF THE CONSCIOUS AND EXAGGERATED MOVEMENTS OF RESPIRATION IN DYSPNŒA.—In ordinary respiration, the sense of want of air, which is the starting point of the stimulus that gives rise to the respiratory acts, is entirely unconscious, and the acts of inspiration are involuntary and automatic. Even when there is a slight deficiency in the proper aëration of the blood, as occurs from the vitiated atmosphere of a crowded room, one experiences merely an indefinite sense of oppression, and the respiratory movements are still of the same involuntary character. But when there occurs any serious interference with the passage of fresh air to the pulmonary vesicles or an obstruction to the flow of arterial blood to the medulla oblongata, as in certain pulmonary and cardiac diseases, the sense of want of air is exaggerated until it becomes a consciousness of pulmonary oppression or impending suffocation. Under such conditions many muscles that are not usually brought into action in inspiration are used, partly by an effort of the will. This is simply an exaltation and extension of the normal respiratory sense, so that it reaches the true centres of sensation, causing a voluntary increase in the number and extent of the inspiratory acts. The sense of suffocation, indeed, differs from the normal unconscious respiratory sense merely in degree and in the fact that the former operates on the centres of ordinary sensation through sensory nerves, while the latter is confined to the medulla oblongata. Having once ascertained definitely the cause of the normal sense of want of air, one can readily understand how an exaggeration of the conditions which give rise to the natural automatic movements of respiration may produce those sensations which attend the various degrees of suffocation. As more remote consequences of asphyxia, there occur insensibility, an arrest of the circulation by engorgement of the heart and finally the sensibility of the medulla oblongata disappears. As

a general rule, when the action of the heart has ceased from asphyxia, even the most efficient artificial respiration fails to restore the respiratory function, for the reason that it is only by the action of the heart that blood can be sent to the medulla. While, however, the heart continues to act, although its contractions may be very feeble, it is within the limits of possibility to revive the functions of the medulla by artificial respiration.

There are certain agents which seem to affect the medulla directly, such as narcotics and anesthetics. In poisoning by opium the frequency of the respiratory acts is diminished and they may be arrested. All experimenters must have frequently observed arrest of respiration by the administration of anæsthetics to animals. In such instances, if the heart continues to beat, it generally is possible to revive the respiratory function by artificial insufflation of the lungs. In most cases of suspended respiratory action from any temporary cause, although electricity, sudden and active stimulation of the surface, etc., may aid in restoration, the main reliance should be upon persistent and efficient artificial respiration.

CAUSE OF THE FIRST RESPIRATORY ACT AFTER BIRTH AND OF RESPIRATORY EFFORTS IN UTERO.—No one doubts, at the present day, that the blood from the placenta furnishes to the foetus in utero all the oxygen demanded for the function of respiration; and it is unnecessary to cite authorities to show that the blood of the umbilical vein contains oxygen, as this fact has long since been established. If the uterus of an animal far advanced in gestation is opened, an experiment which I have frequently made on cats and dogs, the foetuses for a time will make no respiratory efforts; but compression of the umbilical vessels of one will cause it to make very violent movements of inspiration, while the others will remain quiet so long as the placental circulation is not interrupted. The umbilical vein carries its blood to the vena cava ascendens, thence to the left side of the heart through the foramen ovale, and thence to the upper extremities and head, including, of course, the medulla oblongata. Thus the blood that is most highly oxygenated is supplied to the medulla; and the aorta below the arch receives, through the ductus arteriosus, the blood from the right ventricle, which con-

tains a much smaller quantity of oxygen than the blood distributed through the vessels given off above. Cutting off the flow of blood from the placenta is almost equivalent, therefore, to tying the vessels of the arch of the aorta. When this is done, the flow of oxygenated blood to the medulla is arrested; and there follows a sense of want of air which induces a stimulus that is sent to the muscles of inspiration. Air is then for the first time taken into the lungs, and the conditions of the circulation are changed. The lungs are now distended with air, and the pulmonary vessels are dilated, so that the right ventricle supplies the pulmonary capillaries, instead of sending the venous blood, as before, in greatest part through the ductus arteriosus. The pulmonary circulation being thus established, the conditions rapidly assume the character observed in the adult.

It is evident, from the experiments already noted showing the effects of compression of the umbilical vessels, that an abnormal condition in utero, in which there is serious interference with the placental circulation, may induce inspiratory efforts in the foetus, and that the liquor amnii may thus find its way into the air-passages.

ARE THE NORMAL RESPIRATORY MOVEMENTS EITHER ENTIRELY OR IN PART REFLEX, IN THE SENSE IN WHICH THE TERM REFLEX IS ORDINARILY UNDERSTOOD BY PHYSIOLOGISTS?

This question is one which naturally arises as a logical sequence of the experiments I have described and of the deductions that I have drawn from the ascertained facts. The most important of these facts is the following: When the medulla oblongata is freely supplied with oxygen-carrying blood in a living animal, this being effected by artificial insufflation of the lungs, there are no inspiratory efforts. The animal makes respiratory efforts as the supply of oxygen to the medulla diminishes; and the want of oxygen alone is capable of inducing the stimulus to the muscles which gives rise to the efforts to introduce air into the lungs. It is evident that the stimulus, under these experimental conditions, which was formerly thought to be reflex and produced by a certain impression conveyed to the medulla by centripetal nerves, really takes its origin

in the medulla itself; that the respiratory sense, so called, is due to some alteration in the conditions of the medulla, which depends upon the supply of oxygen-carrying blood; and finally, that this alteration does not of necessity involve any impression received through afferent nerves. Viewed in this way, when a living animal, in which the respiratory movements have been for the time arrested by artificial insufflation of the lungs, makes inspiratory efforts following the operation of shutting off the blood-supply from the medulla, the stimulus which gives rise to these efforts can not properly be called reflex.

I shall leave out of the question under consideration various modifications of the respiratory acts, such as coughing, sneezing, etc., and the influence of certain unusual impressions made upon the surface, as by a cold douche, restricting the discussion to the normal respiratory movements.

It is well known that a relatively strong electric current applied to the pneumogastric nerves in the neck or to certain branches of the pneumogastriCS, the superior and the inferior laryngeals, will instantly arrest respiration. This action is reflex, as is shown by the fact that stimulation of the central ends of the divided nerves influences respiration, while the stimulus applied to the peripheral ends has no effect. The effect of powerful electric stimulation of the pneumogastriCS and of certain of their branches is marked and constant; at the same time, stimulation of some of the nerves of general sensibility has been observed to arrest respiratory movements, although this result is not invariable. When the respiratory movements are completely arrested by faradization of the pneumogastriCS, it is always the same for the general movements of the animal, which remains motionless.* On the other hand, "a feeble excitation accelerates the respiration; a more powerful excitation retards it; a very powerful excitation arrests it. These words 'feeble' and 'powerful' having, it is understood, only a relative sense for any one animal, and under certain conditions: what is feeble for one would be powerful for another, etc." †

* Bert, "Leçons sur la physiologie comparée de la respiration," Paris, 1870, p. 490.

† Bert, *loc. cit.*

So far as these experimental facts can be applied to the physiology of ordinary respiration, it seems that the nerves, the action of which is brought into play under physiological conditions, must be mainly if not exclusively the pneumogastrics. These nerves have their origin at the medulla oblongata, which undoubtedly contains the sole respiratory nerve-centre; they are distributed to the entire respiratory apparatus from the larynx to the deepest parts of the lungs; they are the only nerves belonging to the cerebro-spinal system that are distributed to the larynx, trachea, bronchia and the pulmonary parenchyma; while they are not distributed to the respiratory muscles, except the intrinsic muscles of the larynx, they are capable, by reflex action, of exerting a very marked influence over the respiratory movements. In discussing, then, the question of reflex nervous action in normal respiration, the argument may properly be confined to the pneumogastrics.

The curious and interesting respiratory phenomena observed in living animals after section of both pneumogastrics are very important. When both pneumogastrics are divided in the neck, the excitation directly produced by their section momentarily accelerates the respiratory movements. In very young animals, in which the cartilages of the larynx are comparatively soft and pliable, the paralysis of the inferior laryngeal nerves, which preside over the respiratory movements of the glottis, often produces speedy suffocation from closure of the glottis during the inspiratory act; but in most adult animals the walls of the larynx are sufficiently rigid to enable the acts of inspiration to be carried on without serious obstruction. In such animals, for a few seconds, the number of respiratory acts may be increased; but so soon as they become tranquil, the number is very much diminished and the movements change their character. The inspiratory acts become unusually profound and are attended with excessive dilatation of the thorax. Under these conditions I have seen the number of respirations fall from sixteen or eighteen to four per minute.

In discussing the possible reflex influences upon the normal respiratory movements which may operate through the pneumogastrics, I shall make use of a very interesting suggestion made by Rosenbach, in 1878. In a brief note

upon the "Influence of Stimulation of the Vagus upon Respiration," Rosenbach proposes the theory that this nerve (the vagus) is the vasomotor nerve of the medulla oblongata, and that it contains fibres which contract, and fibres which dilate the bloodvessels. This idea is presented by Rosenbach simply as an hypothesis, which he "hopes later to be able to establish by experiments." *

I may now state, in continuing my argument, the following propositions, all of which, except the last, I assume to be facts that have been established experimentally:

I. A deficiency in the quantity of oxygen supplied to the medulla oblongata through the arterial blood circulating in its substance will of itself give rise to a stimulation of the muscles concerned in the act of inspiration.

II. A relatively feeble electric stimulation of the pneumogastric nerves increases the frequency of the inspiratory acts; a stronger stimulation may diminish their frequency; and a very powerful stimulation arrests the respiratory movements. The action in these instances is reflex and not direct.

III. Section of both pneumogastric nerves in the neck, in most adult animals, very greatly diminishes the frequency of the respiratory acts.

IV. The pneumogastric nerves possibly contain vasomotor filaments that are capable of regulating and modifying the supply of blood to the vessels of the medulla oblongata.

If these propositions are taken as the basis of a theory of the mechanism of normal respiration, the following seem to be the natural and logical conclusions to be drawn from them:

I. When the action of the medulla oblongata is removed from the influence of the pneumogastric nerves, as it is after division of both of these nerves in the neck, air is taken into the lungs when the deficiency of oxygen in the medulla has reached the point at which the respiratory sense necessarily generates the stimulus sent to the inspiratory muscles. This action is in no sense reflex, and it depends entirely upon the development, *de novo*, of a stimu-

* Rosenbach, "Notiz über den Einfluss der Vagusreizung auf die Athmung."—"Archiv für die gesammte Physiologie," Bonn, 1878, Bd. xvi., S. 503.

lation or an irritation in the medulla itself. Under these conditions the acts of inspiration are abnormally infrequent and they become excessively prolonged and profound.

II. In normal respiration, however, it is certain that important reflex influences operate upon the medulla oblongata through the pneumogastric nerves. While there can be no doubt that the stimulus which gives rise to inspiratory efforts is due purely and simply to want of oxygen in the medulla, in order that this stimulus shall operate in accordance with the requirements of the system for oxygen, producing normally sixteen to twenty inspirations per minute and varying the number of these movements with different physiological conditions of the organism, depending upon muscular exercise, etc., it is necessary that the respiratory acts should be regulated through the nervous system. Inasmuch as the respiratory acts involve the contraction of striated muscular fibres, it would be expected that the nerves which regulate them should belong to the cerebro-spinal system. In studying experimentally the influence of various nerves on the respiratory movements, it is found that the pneumogastrics, which arise from the medulla and are distributed largely to the respiratory apparatus, are closely connected with certain artificially-induced modifications of respiratory action. By applying to these nerves electric stimulation of different degrees of intensity, the respiratory movements may be increased or diminished in frequency or they may be arrested, and these phenomena are always reflex.

III. Section of both pneumogastric nerves seems to remove the medulla oblongata, so far as its action as a respiratory nervous centre is concerned, from the reflex action of the nervous system; and the respiratory acts then become so far diminished in frequency and are so laboured as to produce serious pulmonary lesions. It is probable that death occurs in a few days after this operation, not alone from abnormal respiratory action but from a suspension of other important functions which the pneumogastrics have to perform. It is possible, also, that some of the phenomena that are observed in narcotic poisoning, notably the great diminution in the number of respiratory movements, are due to an interference with the respiratory functions of the pneumogastrics.

The precise mechanism of the action of the pneumogastrics in normal respiration and the exact seat and character of the impressions which serve as the starting point in the reflex phenomena observed, it is difficult to describe within the limits of ascertained facts. If the theory advanced by Rosenbach is accepted; viz., that the pneumogastrics contain vasomotor filaments which regulate the quantity of blood passing through the medulla oblongata, the mechanism of the action which takes place in the respiratory nerve-centre is readily understood; but the seat and the exact nature of the impression which gives rise to these reflex changes in the calibre of the vessels are still a matter of speculation and conjecture. So far as muscular action in tranquil respiration is concerned, it is necessary to consider only the acts of inspiration, for expiration is produced mainly by the passive reaction of the walls of the thorax and by the resiliency of the elastic pulmonary parenchyma succeeding the action of the muscles which enlarge the chest and inflate the lungs.

Finally, the respiratory sense, "*besoin de respirer*," sense of want of air, or the stimulus which gives rise to inspiratory efforts, is due purely and simply to a deficiency in oxygen in the medulla oblongata, in which is contained the sole respiratory nerve-centre. The frequency and the extent of the normal inspiratory movements are regulated and accommodated to the physiological requirements of the system by reflex action operating through the pneumogastric nerves.

In this article I have endeavored to set forth the nature and the physiological bearings of my experiments, published in 1877, showing that the sense of want of air is due primarily to a deficiency of oxygen in the medulla oblongata. I have attempted, also, to show how the operation of the stimulus to the inspiratory muscles, which is due to this deficiency of oxygen in the medulla, is regulated, in normal respiration, by reflex action through the pneumogastric nerves. Physiologists are now well acquainted with the action of the pneumogastrics in connection with the circulation, the action of the stomach and intestines and certain functions of the liver; but the action of these nerves in normal respiration and the causes of the

respiratory phenomena following their stimulation and their section have heretofore been obscure. I venture to hope that my discussion of the reflex function of the pneumogastrics in connection with the respiratory movements has thrown some light upon questions which have not been satisfactorily answered by physiologists.

IX

EXPERIMENTAL RESEARCHES INTO A NEW EXCRETORY FUNCTION OF THE LIVER; CONSISTING IN THE REMOVAL OF CHOLESTERIN FROM THE BLOOD, AND ITS DISCHARGE FROM THE BODY IN THE FORM OF STERCORIN. (THE SÉROLINE OF BOUDET.)*

ILLUSTRATED BY THREE PLATES CONTAINING FIFTEEN
FIGURES

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"La cholestérine du sang est elle un de ces produits destinés à être expulsés de l'économie, et, par conséquent, dépourvus d'action immédiate sur l'économie elle même? Sa destination est tout à fait inconnue." "Traité de physiologie," par F. A. Longet. Paris, 1861. Tome i., p. 488.

THIS sentence, which is taken from the most elaborate treatise on physiology in any language, published at the centre of physiological science, in 1861, expresses the state of our knowledge in regard to the function of cholesterolin. Cholesterolin was discovered in 1782, by Poulletier de la Salle, in biliary calculi, and was detected upwards of thirty years ago in the blood by Denis; but since then, with the exception of researches of a purely chemical nature into its properties, our knowledge in regard to it has not advanced. Its chemical history even, is far from perfect; while its physiological history is unknown. In 1833

* A French translation of this essay was published in Paris in 1868, and in 1869 received an "honorable mention" with a "recompense" of 1,500 francs from the Institute of France (Académie des Sciences), Concours Monthyon (Médecine et Chirurgie), being second to the essay of Villemain (Études sur la tuberculose, preuves rationnelles et expérimentales de sa spécificité et de son inoculabilité), which work received the Monthyon prize for that year.

Boudet discovered a substance in the blood which he called "séroline"; a principle having many characters in common with cholesterin, but heretofore interesting merely as a curious proximate principle, found in excessively minute quantities in the serum of the blood only (whence its name); too minute, indeed, for ultimate analysis. Its function was as obscure as that of cholesterin. In examining the literature of these two substances, I find that cholesterin is frequently not treated of in systematic works on physiology. Serolin is seldom even mentioned. Their function has been so obscure and apparently so unimportant, that theories in regard to it have not been advanced; and the highest chemical authorities, in speaking of their office in the economy, simply say of one, as of the other, that it is unknown. In the "Chimie anatomique," by Robin and Verdeil, I find cholesterin summed up in these words:

"Le rôle physiologique qu'elle remplit dans l'économie est également inconnu."

Of serolin, the same authors say:

"On ne sait pas comment se forme la séroline, ni quel est son rôle physiologique."

Though the physiology of these substances is thus obscure, though chemistry has thus far done but little for their history, and physiology nothing, certain facts with relation to them would seem to indicate that they are not unimportant in the economy. Cholesterin is found in the blood, bile, liver, nervous matter, crystalline lens, meconium (not in the feces, as incorrectly stated by authors), beside in a number of morbid products. It is found in these situations constantly; it appears in the blood as soon as that fluid is found, and continues to the end of life. Its quantity in the blood is increased in certain diseased conditions and diminished in others. Serolin has been said to exist constantly in the blood, though, till now, it has never been discovered in any other situation. It, like cholesterin, is a constant principle, they having many chemical characters in common. Their function is definite; it is important; and, if the writer does not exaggerate this importance in the enthusiasm of exploring a hitherto absolutely uncultivated field, a knowledge of the functions of these substances will be of incalculable value to the practical physi-

cian; and the path thus opened by physiology will lead to a great field for pathological inquiry. What the discovery of the function of urea has done for diseases which now come under the head of uremia, the discovery of the function of cholesterin may do for the obscure diseases which may hereafter be classed under the head of cholesteremia.

It is not surprising that the function of substances—which have been isolated with great difficulty, which have never been found in any of the excretions, which exist in quantity so small that their investigation seemed to belong especially to the chemist, physiologists having been discouraged, perhaps, from studying them—should be thus obscure. But it is surprising that an important fluid, the bile, the product of the largest gland in the economy and the one most constantly found in the animal scale, should be so little understood. This has been regarded by some as a simple excrement, and by others as not an excrementitious, but a digestive fluid; and so much labor has been expended by physiologists in endeavors to settle this point, that no one has pretended to give an account of its excrementitious function, if it has any, and researches into its digestive function have left us almost entirely in the dark. Blondlot reported an observation on a dog that lived for five years with a biliary fistula diverting, as it is stated, all the bile from the intestines and discharging it from the body. The animal presented no untoward symptoms, died a natural death, no bile found its way into the intestines, but it was all discharged. According to this observation, the bile would appear to be purely an excretion. Schwann, and Bidder and Schmidt, in a large number of experiments, never succeeded in keeping a dog operated on in this way for more than a few weeks; they all died with evidences of inanition. The bile, according to these observations, is concerned chiefly in nutrition; and as it is poured into the upper part of the digestive tube, it is important, probably, in digestion. But Bidder and Schmidt do not satisfy us what its digestive function is; nor does Blondlot say what principle is excreted by it or what would be the result of its suppression.

Aside from a few isolated facts, interesting enough, but indicating nothing definite, this is all we know of the function of the bile. But what physiologist does not feel

this hiatus in his science; or what practical physician does not feel and know the importance of the function of the bile! It needs no inquiry into natural history, showing the universality, almost, of the liver in the animal scale, to impress upon the physician at the bedside the importance of the bile. A patient is suffering from an obscure ailment, which he may call biliousness or derangement of the liver, and which, in some unexplained way, is relieved by a mercurial purge. The practitioner knows that the bile-secreting function of the liver is important, but does not learn it from the physiologist. Every practitioner must feel that the liver has a function which must be explained him by the physiologist, before he can avoid treating a large class of diseases empirically.

The bile has an important excretory function, which is liable to many disorders; and this function I hope to be able, in the present article, to describe.

It is evident from the preceding remarks that the physiological history of the bile remains to be written. The subject is too interesting and important not to engage the mind of the experimental physiologist. It is difficult at first sight to harmonize statements, to which reference has just been made, of experimenters, equally entitled to consideration, which are diametrically opposite. But of course the philosophical method of studying the bile is first to settle whether it is excrementitious or recrementitious. If the former, what substance is excreted, and where is it formed? If the latter, what function does it perform in any of the processes of nutrition. With the view to harmonize, if possible, in my own mind, the opposite statements of Bidder and Schmidt and of Blondlot, I attempted some time ago to establish biliary fistulæ in dogs. The first experiments were made in New Orleans in the winter of 1860-61, but were all of them unsuccessful, no animal surviving the operation more than three days. The experiments were discontinued at that time but were renewed in the winter of 1861-62 at the Bellevue Hospital Medical College. After a number of trials which were no more successful than those made the previous winter, I succeeded in performing the operation with considerable rapidity and with very little disturbance of the abdominal organs, and in one animal the success was complete.

EXPERIMENT I.—The operation was performed by making an incision into the abdomen in the median line just below the ensiform cartilage, about three inches in length. The edge of the liver was carefully raised, the bile duct isolated, and two ligatures applied, one next the duodenum and the other near the junction of the ductus choledochus with the cystic duct, the intermediate portion being excised. The fundus of the gall-bladder was then drawn to the upper part of the wound, an incision made in it of about an inch in length, the bile evacuated, and the edges attached to the skin by points of interrupted suture. The wound was then carefully closed around the opening into the gall-bladder.

This is nearly the proceeding recommended by Blondlot, who prefers, however, to operate while the animal is fasting, as the gall-bladder is then distended and can be easily found. I have preferred to operate after feeding, when the gall-bladder is comparatively empty, as there is no great difficulty in finding it, and in evacuating its contents less bile is likely to find its way into the peritoneal cavity, which is one of the causes of the intense peritonitis which follows this operation.

The animal ate well the day after the operation, the bile flowed freely from the fistula and was entirely cut off from the intestine, as shown by post-mortem examination. No symptoms supervened except those produced by the diversion of the bile from its normal course. This operation was performed on the 15th of November, 1861, and the animal lived thirty-eight days.

In no observation that I have found recorded has the animal been so free from inflammation consequent upon so serious an operation; and this seemed a most favorable opportunity for determining whether an animal could live with the bile shut off from the intestinal tube and discharged by a fistula. In this case the animal gradually lost flesh and strength, his appetite becoming voracious, until finally he died of inanition; the observation agreeing in every important particular with the experiments of Schwann, and of Bidder and Schmidt.

EXPERIMENT II.—This experiment was undertaken to ascertain, if possible, the entire quantity of bile secreted in twenty-four hours. A fistula was made into the ductus communis choledochus, the duct being divided and a silver tube introduced. The experiment did not succeed in the point of view in which it was undertaken, and about forty-eight hours after the operation, the tube dropped out. After the removal of the tube the bile ceased to flow externally, and the animal did not appear to suffer any bad effects from the experiment. Thirty days after the operation, the animal having entirely recovered, he was killed by section of the medulla oblongata, and the parts carefully examined. The post-mortem examination I transcribe from my note-book.

“On post-mortem examination the liver was found adherent to the diaphragm over the greater part of its convex surface. There were evidences of limited inflammation over the duodenum. The liver itself was normal. Upon opening the duodenum, the papillæ which marks the opening of the ductus communis chole-

dochus was normal in appearance. A small silver stilet was introduced into the duct. For a long time it was impossible to find any communication between the upper part of the duct and the intestine; but at last, after patient searching (knowing that no bile was discharged from the body and that it was absolutely certain that a communication existed with the duodenum), a communication was found. In Blondlot's case there probably was a communication reestablished which escaped his observation."

In the remarkable observation reported by Blondlot, in which the animal survived for so long a period, the success is attributed to the fact that the dog was prevented from licking the bile as it flowed from the fistula, Blondlot stating that so soon as the animal was prevented from licking the bile, nutrition began to improve. Anxious to carry out all the precautions which had been adopted, I so muzzled the animal in Experiment I., covering the lower part of the muzzle with oiled silk, that it was impossible for him to swallow a drop of the bile. This muzzle was kept on till the death of the animal, but the proceeding had no effect on his nutrition. The bile flowed so freely from the fistula that all the lower part of the animal was covered with it. It was not, however, until I made the post-mortem examination in the second experiment that I was able to see the difficulty which I had experienced in harmonizing the observations of the different experimenters I have quoted. In the lower animals—in dogs, at least—ducts have a remarkable tendency to reestablish themselves. Any one who has operated much upon the glands can hardly fail to have noticed this fact. The pancreatic duct, for example, after having been divided and a tube introduced, invariably becomes reestablished after the simple removal or dropping out of the tube. It was so in Experiment II., in which the tube dropped out of the bile duct. The duct undoubtedly became reestablished, for no bile flowed externally for nearly a month, the animal enjoying perfect health, and the fluid necessarily being emptied into the intestine; yet it was with the greatest difficulty that the communication could be found with the probe, and it was only after long searching, knowing that there must be a communication, that it was discovered at all. Taking into consideration the great difficulty I had in finding the passage in this instance, and after having carefully examined the case reported by Blondlot, I have

concluded that a communication existed in his experiment which escaped observation, but by means of which a large quantity of bile found its way into the intestine.*

In regard to the digestive function of the bile, it is sufficient to state here that the experiments which I have made on this subject have led me to believe that this fluid has an important office in connection with the function of digestion—one, indeed, which is essential to life. The nature of its office, however, is not understood and can be settled only by a long and carefully executed series of experimental researches which would probably involve the whole subject of digestion. This I hope to be able to present in another paper. There is, however, another function of the bile entirely distinct from the preceding. It is the separation from the blood of cholesterin, an excrementitious substance, which is formed by the destructive assimilation of certain tissues of the body. Though not discharged from the body as cholesterin, it being first changed into another substance, it is separated in that form from the blood and poured into the intestine by the ductus communis choledochus. This new excretory function of the bile will form a great part of the subject of this paper; the recrementitious function, which is necessary to complete the physiological history of this fluid, being deferred.

It will be found that cholesterin is the most important excretion separated by the liver, as urea is the most important excretion separated by the kidneys; and the study of this substance will necessarily involve the depurative function of the liver. I shall therefore begin with cholesterin, and endeavor to show where it is formed in the economy, by following the blood in its passage through various organs. This will necessarily involve a description of the chemical processes which have been employed in its extraction. I shall then endeavor to show where the

* An account of this experiment is to be found in an article entitled "*Essai sur les fonctions du foi et de ses annexes*," par N. Blondlot, 1846. The post-mortem examination of the animal, made more than five years after the establishment of the fistula, was published in a little memoir complementary to the preceding, entitled "*Inutilité de la bile dans la digestion*," 1851. It is not contemplated to enter into a full discussion of the views of Blondlot and others on the uses of the bile in digestion. That subject will be taken up in another paper in which mainly the digestive properties of the bile will be considered. In this connection it is proposed to take up only the excrementitious function of the bile.

cholesterin is removed from the blood, by the same method of investigation. The next step will be to follow it out of the body and study the change which it undergoes in its passage through the alimentary canal. Having described the process of formation in the tissues, separation from the blood by the liver and final discharge from the body, I shall endeavor to show, finally, the effects of interruption of this function of the liver upon the economy. This will lead into pathology, and a host of diseases will arise which may be dependent on a disturbance of the excretory function of the liver. I shall be enabled to draw the line more closely between conditions in which there is resorption simply of the innocuous coloring matter of the bile, and those diseases in which there is a failure to separate the excretions from the blood. These conditions, it is well known, are widely different as to gravity, and the distinction between them is of great importance. The latter condition, characterized by the retention of cholesterin in the blood, will be treated of under the name of cholesteremia.

CHOLESTERIN

CHEMICAL CHARACTERS.—Cholesterin is a non-nitrogenous substance, having all the properties of the fats, excepting that of saponification with the alkalies. Its chemical formula is usually given as $C_{25}H_{42}O$. It belongs to a class of fatty substances which are non-saponifiable, which have been grouped by Lehmann under the name of lipoids. This class is composed of cholesterin and serolin, which are animal substances; castorin, from the castoreum, and ambrein, from amber. To this he adds a substance discovered in a uterine tumor by Busch, called inosterin. Cholesterin is neutral, inodorous, crystallizable, insoluble in water, soluble in ether, very soluble in hot alcohol, though sparingly soluble in cold. It burns with a bright flame, but is not attacked by the alkalies, even after prolonged boiling. When treated with strong sulphuric acid, it strikes a peculiar red color, which is mentioned by some as characteristic of cholesterin. I have found that it possesses this character in common with serolin.*

* This reaction of serolin is mentioned by Bérard, in his "Cours de physiologie," tome iii., p. 117.

FORMS OF ITS CRYSTALS.—Cholesterin may easily and certainly be recognized by the form of its crystals, the characters of which can be made out by means of the microscope. They are rectangular or rhomboidal, exceedingly thin and transparent, of variable size, with distinct and generally regular borders, and frequently arranged in layers with the borders of the lower crystals showing through those which are superimposed. This arrangement of the crystals takes place when cholesterin is present in considerable quantity. In pathological specimens they generally are few in number and isolated. The plates of cholesterin are frequently marked by a cleavage at one corner, the lines running parallel to the borders; frequently they are broken, and the line of fracture is generally undulating. Lehmann attaches a great deal of importance to measurements of the angles of the rhomboid. According to this author, the obtuse angles are $100^{\circ} 30'$, and the acute $79^{\circ} 30'$. I have lately examined a great number of specimens of cholesterin, extracted from the blood, bile, brain, liver, and occurring in tumors, and am confident that the crystals have no definite angle. Frequently the plates are rectangular, and sometimes almost lozenge-shaped. It is by the transparency of the plates, the parallelism of their borders, and their tendency to break in parallel lines that we recognize them as formed of cholesterin. Lehmann seems to consider the tablets of this substance as regular crystals having invariable angles. From examination during crystallization, I am disposed to think that they are not crystals but fragments of micaceous sheets, which, from their extreme tenuity, are easily broken. In examining a specimen from the meconium, which I extracted with hot alcohol, I was able to see a transparent film forming on the surface of the alcohol soon after it cooled; this, on microscopic examination, in situ, disturbing the fluid as little as possible, was found to be marked by long and parallel lines. When the fluid had partially evaporated, it became broken and took the form of the ordinary crystals of cholesterin, but they were larger and more regular. The beauty of the tablets at this stage could not be adequately represented. They were exceedingly thin, and regularly divided into delicate plates, with the characteristic corner cleavages of cholesterin; and

as the focus of the instrument was changed, new layers, with different arrangement, were brought into view. I have attempted to give an idea of the form of these tablets in Fig. 1; but it is, of course, impossible to represent their pale, but beautifully distinct borders. As has been remarked by Robin, the borders of these crystals can be but imperfectly imitated by a line; there is no line in the object itself, but the edge shows where the tablet ceases. (See Fig. 1.)

The crystals generally are colorless, but when present in colored fluids, may take a yellowish tint or even become very dark. They may still be recognized, however, by the characters of form just described.

Crystals of cholesterin melt at 293° Fahr., but are formed again when the temperature falls below that point. According to Lehmann, they may be distilled in vacuo at 680° without decomposition. The determination of the fusing point is one of the means of distinguishing it from serolin, which fuses at 90.8° .

SITUATIONS OF CHOLESTERIN.—Most authors state that cholesterin is found in the bile, blood, liver, brain and nerves, crystalline lens, meconium and the fecal matter. I have found the cholesterin in all these situations invariably, excepting the feces, where it was seen but once after a number of examinations; and in studying the works of those who have investigated this substance, I can find no one who has found it in the normal feces. It is found in large quantities in the meconium, from which, perhaps, it is most easily extracted in a state of purity, and has been extracted from the feces of animals in a state of hibernation; but though it may occasionally be found in the feces in disease and in animals after long fasting, I am confident that it never occurs under ordinary conditions. The analysis of the fecal matter is so unattractive that it has been very much neglected by chemists; and until a few years ago, when an elaborate analysis was made by Marcet, to which reference will hereafter be made, the analyses of Berzelius furnished nearly all our data on this subject. Cholesterin forms the greatest part of biliary calculi, which indeed consist generally of nothing but cholesterin, coloring matter and mucus. It is found in a large number of morbid deposits. Few specimens of cancer are examined with-

out discovering tablets of cholesterin. It is very abundant in encysted tumors. According to Robin, atheromatous deposits, which are found in the middle coats of the arteries, are often composed of cholesterin. It sometimes forms distinct tumors or deposits in the substance of the brain. I lately had an opportunity of examining a tumor from the brain, at the Bellevue Hospital, which consisted of nearly pure cholesterin. It has often been found in the fluid of hydrocele, in the fluid of ovarian cysts, in crude tubercle, in epithelial tumors and in pus. The proportion in which it exists in the fluids of the body is very small. I have made a number of quantitative analyses of the blood, the results of which I give in the following table with some other analyses which have been made for this substance. I also give the quantity which I have found in the other situations in which it exists. The variations in different parts of the circulation and in diseased conditions will be given in another table. The quantity in the brain and crystalline lens has, I believe, never before been estimated:

TABLE OF QUANTITY OF CHOLESTERIN IN VARIOUS SITUATIONS

SITUATION.	Observer.	Quantity examined.	Cholesterin per 1,000 pts.
		grains.	
Venous blood (male).....	Becquerel and Rodier.	0.090
“ (female).....	Becquerel and Rodier.	0.090
“ (male set. 35).	Flint.	312.083	0.445
“ (male set. 22).	Flint.	187.843	0.658
“ (male set. 24).	Flint.	102.680	0.751
Bile (human).....	Frerichs.	1.600
“ (normal, of ox).....	Berzelius.	1.000
“ (human).....	Flint.	224.588	0.618
Meconium.....	Simon.	160.000
“.....	Flint.	170.541	6.245
Brain (human).....	Flint.	159.753	7.729
“.....	Flint.	150.881	11.456
Crystalline lens (ox) *.....	Flint.	135.020	0.907

FORMS UNDER WHICH CHOLESTERIN EXISTS IN THE ORGANISM.—In the fluids of the body cholesterin exists in a state of solution, but by virtue of what constituents it is held in solution is not entirely settled. It is stated that the biliary salts have the power of holding it in solu-

* In this examination four fresh crystalline lenses of the ox were used.

tion in the bile, and that the small quantity of fatty acids which are contained in the blood hold it in solution in that fluid, but direct experiments on this point are wanting. In the nervous substance and in the crystalline lens it is united, "molecule à molecule," to the other elements which go to make up these tissues. After it is discharged into the intestinal canal, when it is not changed into stercorin, it is to be found in a crystalline form, as in the meconium and in the feces of animals in a state of hibernation. In pathological fluids and in tumors it is found in a crystalline form and may be detected by microscopic examination.

PROCESS FOR THE EXTRACTION OF CHOLESTERIN.—Without describing the processes which have been employed by other observers for the extraction of cholesterol from the blood, bile and various tissues of the body, I shall confine myself to a description of the process which I have found most convenient to employ in the analyses I have made for this substance. In analyses of gall-stones the process is very simple; all that is necessary being to pulverize the mass and extract it with boiling alcohol; filter the solution while hot, the cholesterol being deposited on cooling. If the crystals are colored, they may be redissolved and filtered through animal charcoal. This is the proceeding employed by Poulletier de la Salle, Fourcroy and Chevreul. It is only when this substance is mixed with fatty matters that its isolation is a matter of any difficulty. In extracting cholesterol from the blood I have operated on both the serum and clot, and in this way have been able to demonstrate it in greater quantities in this fluid than have been observed by others, who have employed only the serum. The following is the process for quantitative analysis, which I fixed upon after a number of experiments.

The blood, bile or brain, as the case may be, is first carefully weighed, then evaporated to dryness over a water-bath, and carefully pulverized in an agate mortar, so as to collect every particle. The powder is then treated with ether, in the proportion of about a fluidounce for every hundred grains of the original weight, for twelve to twenty-four hours, agitating the mixture occasionally. The ether is then separated by filtration, throwing a little fresh ether on the filter so as to wash through every

trace of the fat, and the solution is set aside to evaporate.* If the fluid, especially the blood, has been carefully dried and pulverized, when the ether is added it divides it into a very fine powder and penetrates every part. After the ether has evaporated, the residue is extracted with boiling alcohol in the proportion of about a fluidrachm for every hundred grains of the original weight of the specimen, filtered, while hot, into a watch-glass and allowed to evaporate spontaneously. To keep the fluid hot while filtering, the whole apparatus may be placed in the chamber of a large water-bath, or as the filtration is generally rapid, the funnel may be warmed by plunging it into hot water, or steaming it, taking care that it be carefully wiped. We now have the cholesterin mixed with a certain quantity of saponifiable fat. After the fluid has evaporated, we can see the cholesterin crystallized in the watch-glass, mingled with masses of fat. This we remove by saponification with an alkali; and for this purpose, we add a moderately strong solution of caustic potash, which we allow to remain in contact with the residue for one to two hours. If much fat is present, it is best to subject the mixture to a temperature a little below the boiling point; but in analyses of the blood this is not necessary. The mixture is then to be largely diluted with distilled water, thrown upon a small filter, and thoroughly washed till the solution which passes through is neutral. We then dry the filter, and fill it up with ether, which, in passing through, dissolves out the cholesterin. The ether is then evaporated, the residue extracted with boiling alcohol as before, the alcohol collected on a watch-glass previously weighed, and allowed to evaporate. The residue consists of pure cholesterin, the quantity of which may be estimated by weight.

The accuracy of this process may be tested by means of the microscope. As the crystals have so distinctive a form under the microscope, it is easy to determine by examining the watch-glass that it has been obtained in a state of purity. In making this analysis quantitatively it is necessary to be very careful in all the manipulations; and for determining the weight of such minute quantities, an accu-

* The ether may be preserved by distillation, instead of allowing it to evaporate, but with the small quantity usually employed this is hardly worth while.

rate and delicate balance, one, at least, that will turn with the thousandth of a gramme, carefully adjusted, must be employed. With these precautions the quantity of cholesterolin in any fluid or solid may be determined with perfect accuracy. The quantity of cholesterolin may be estimated in fifteen or twenty grains of blood. In analyzing the brain and bile I found it necessary to pass the first ethereal solution through animal charcoal to get rid of the coloring matter. In doing this the charcoal must be washed with fresh ether till the solution which passes through is brought up to the original quantity. The other manipulations are the same as in examinations of the blood. In examining the meconium I found that the cholesterolin which crystallized from the first alcoholic extract was so pure that it was not necessary to subject it to the action of an alkali.

I am aware that in describing the process for the extraction of cholesterolin I have entered into details which would be superfluous for the practical chemist. But the extraction of this substance from the blood is so simple, and the results of the examination of blood in different parts of the circulatory system have been so striking and important, that I can not but indulge the hope that the observations which follow will be verified by those who may not be skilful practical chemists. Almost any one is competent to make a quantitative analysis of the blood for cholesterolin. It simply requires six days for the process, and a number of analyses may be carried on at the same time. It requires one day, after the blood has been dried and pulverized, for the ether to act upon it; the next morning it is filtered and set aside; the next morning it will be dry and may be extracted with alcohol and set aside to evaporate; the next morning it may be treated with potash, filtered, and the filter washed with water; the following day it may be washed with ether and set aside to evaporate; the following day it will have evaporated and may be extracted with hot alcohol; and the following day the alcohol will have evaporated and the specimen may be examined by the microscope and weighed. All that is required is a little care in the performance of these simple manipulations—which one with a slight acquaintance with operations in chemistry may perform at once, and one or

two trials will enable a novice to execute—and accuracy in weighing, which is, indeed, the most delicate part of the process.

HISTORY OF CHOLESTERIN.—A brief sketch of the history of this substance may not be uninteresting. It was first obtained by Poulletier de la Salle, in 1782, who extracted it from a biliary calculus. He communicated his observations to Fourcroy, who published them, after having verified his experiments, the death of the discoverer preventing him from making his observations public. Afterward, in examining an old hardened liver, Fourcroy found a concrete oily substance analogous to that discovered by Poulletier. He imagined that the liver had become changed into a substance resembling spermaceti. Cholesterin was afterward found in gall-stones, by Vicq d'Azyr, Jaquin, Titius and Kreysig. In 1791 Fourcroy described a substance which he called adipocire, found in bodies at the Cimetière des Innocents, which he likened to spermaceti and to cholesterin. He always, however, made a distinction between these substances; calling cholesterin crystallizable adipocire. In 1814 Chevreul established the difference between adipocire and cholesterin, giving a full description of the cholesterin. He extracted it from the bile of the human subject, of the bear and of the pig.

After that time a number of chemists found it in gall-stones and in intestinal concretions. Lassaigne found it in a cerebral tumor, Guérard in hydatid cysts of the liver, Morin in the liquid from an abdominal tumor, Caventou in the matter from an abscess under the malar bone, and a number of others in tumors in various situations. In 1830 it was discovered in the blood by Denis, and afterward described by Boudet, who wrote an elaborate article on the composition of the serum of the blood in 1833, in which he described cholesterin and a new substance which he called séroline.* It was also detected in normal blood by Lecanu and Marchand. Couerbe, who made elaborate researches into the chemical composition of the cerebral substance, pointed out the existence of cholest-

* Boudet, "Nouvelles recherches sur la composition du serum du sang humain."—"Annales de chimie et de physique," tom. lii., p. 337.

terin in the brain. Lebert found it in the substance of cancerous tumors, Curling found it in the fluid of hydrocele, Simon extracted it from the meconium and Preuss discovered it in the substance of crude tubercle. Of late authors, Becquerel and Rodier have been most extended in their investigation of this principle.* They have made a number of careful quantitative analyses of the blood for this substance in health and disease. Their observations will be more particularly referred to farther on.†

FUNCTIONS OF CHOLESTERIN.—By experiments which I have performed upon the lower animals and by certain facts which have been developed by observations on the human blood in health and disease, I think I have been enabled to solve the problem of the function of cholesterin.

Cholesterin is an excrementitious product, formed in great part by the destructive assimilation of the brain and nerves, separated from the blood by the liver, poured into the upper part of the small intestine with the bile, transformed in its passage down the alimentary canal into stercorin (the séroline of Boudet, a substance differing very little from cholesterin), and, as stercorin, discharged by the rectum.

The quotation with which I prefaced this paper expresses the actual state of knowledge in regard to cholesterin. Still, though our actual knowledge of its function has been so slight, a few writers on chemical physiology and on physiology, taking the limited data on this subject, make reference to it as an effete substance. In regard to its relation to the brain, some think that it is formed in the brain and taken up by the blood, while others think that it is formed in the blood and deposited in the brain. All the views in regard to its effete properties are of course based on the supposition that it is discharged in the feces. Effete matters are discharged from the body, and this would find its exit by the anus, since it has never

* "Traité de chimie pathologique appliquée à la médecine pratique," par M. Alf. Becquerel, Professeur agrégé, etc., et par M. A. Rodier, Docteur en Médecine, etc., Paris, 1854, and "Recherches sur la composition du sang," Paris, 1844.

† The history of cholesterin was compiled mainly from Robin and Verdeil, the "Chimie anatomique."

been detected in the urine. These conjectures have attracted little attention in the scientific world; and these views being based on the supposition that this substance is found in the fecal matters, fall to the ground from the fact that no one as yet detected it in the feces. The fact that cholesterin is so generally considered an ingredient of the feces may be thus explained. It is poured into the alimentary canal with the bile; no one has shown what becomes of it, the chemistry of the feces being little understood; and therefore it has been assumed that it is found in the feces. That the facts which we have with regard to cholesterin render its effete properties possible, and perhaps probable, is certainly true; but these facts are merely sufficient to enable the scientific investigator to address an intelligent inquiry to Nature on this subject; they do not solve the question. In the experiments which form the basis of this article, the inquiry was made and the answer obtained; some others have, without much reflection apparently, made simple statements which approximate in some degree to the facts. The only way these assertions could be sustained is by the labor which I have expended in eliciting from Nature a reply to my interrogatories.

The works which I have had an opportunity of consulting where any decided opinion relative to the function of cholesterin has been expressed, are those of Carpenter, Lehmann, Mialhe and Dalton.*

Carpenter, in the fifth American edition of his "Human Physiology," 1853, has the following in regard to the function of cholesterin:

"It is also stated to be a constituent of the nervous tissue, having been extracted from the brain by Couerbe, and other experimenters; but it may be doubted whether this is not rather a product of the disintegration of nerve-substance, which is destined to be taken back into the blood for elimination by the excretory apparatus, like the kreatine which may be extracted from the juice of flesh, or the urea which is obtainable from the vitreous humor of the eye, both being undoubtedly excrementitious matters. For cholesterin is a characteristic component of the biliary excretion, and is closely related to its peculiar acids; so that it can scarcely be looked upon in any other light than as an excrementitious prod-

* These authors are quoted in the order in which their publications appeared.

uct, the highest function of which is to assist in the support of the calorifying process. It is frequently separated from the blood as a morbid product; thus it is often present in considerable quantity in dropsical fluids, and particularly in the contents of cysts; and it may be deposited in the solid form in degenerated structures, tubercular concretions, etc." *

In Lehmann, I find the following on this subject:

"Judging from the mode of its occurrence, we must regard it as a product of decomposition; but from what substances and by what processes it is formed, it is impossible even to guess. Notwithstanding the similarity which many of its physical properties present to those of the fats, we can hardly suppose that it takes its origin from them, since the fats, for the most part, become oxidized in the animal body, whereas in order to form cholesterin, they must undergo a process of deoxidation." †

I translate the following from Mialhe, on "Chemistry applied to Physiology and Therapeutics," Paris, 1856, the paragraph entitled "Source of Cholesterine in the Animal Economy."

"We have just examined in what manner the fatty bodies penetrate into the blood. Some eminent savans have held that the fatty matters from the exterior are the only ones which exist in the economy, and that it is incapable of producing these in itself. Now it is an opposite opinion which tends to predominate, and the majority of physiologists think that certain fatty bodies take origin in the very substance of our organism. This last mode of origin seems at least incontestable for the cholesterine, which has not yet been found in the vegetable kingdom.

"But what are the chemico-physiological reactions which preside over the development of this particular fatty substance?

"There are for us two modes for comprehending the formation of the cholesterine at the expense of the elements of the blood. Cholesterine may come from the fatty matters; it would be, in this case, like the final result or last stage of chemical modifications which the fatty matters undergo in the animal economy.

"This manner of viewing it is slightly probable; for, in order that it should be true, it would be necessary that the fatty bodies, in oxidizing, should give rise to a compound richer than they in carbon. We know, indeed, that cholesterine is, of all fatty bodies, the one which contains the most carbon.

"We think that we should reject that opinion and stop at the following.

"The production of cholesterine may be attributed to a transformation of the albuminoid materials, a transformation analogous

* Carpenter, "Principles of Human Physiology," Philadelphia, 1853, p. 74.

† "Physiological Chemistry," by Professor C. G. Lehmann, Philadelphia, 1855, vol. i, p. 248.

to that which has been pointed out by M. Blondeau de Carrolles in cheese, and which that chemist has designated under the name of adipose fermentation. The large proportion of carbon which the cholesterine contains, and which approximates it to albuminous matters, would come to the support of that point of view. The retardation of the circulation, and the deficiency of oxidation which is the consequence of it, explains also why the cholesterine is in much greater proportion in the closed cavities than in the blood itself.

"Whichever it may be of these two opinions, it is incontestable for us that, if the cholesterine is not burned with the other matters proper to respiratory alimentation, it is solely on account of its chemical inertia; cholesterine, indeed, is to fatty matters what mannite is to saccharine substances—what urea is to albuminoid matters; that is to say, that it constitutes a kind of *caput mortuum*, of which the organism has only to free itself. It is certain also, for us, that if the cholesterine is not found in all the excrementitious liquids, where most of the other products existing in the blood are found, it is solely on account of its insolubility.

"The preceding remarks explain perfectly, to our eyes at least, why the presence of cholesterine has never been established in the urine of man, either in the form of crystals, or '*calculi*,' while this substance is found in the bile, where it very often forms calculi of considerable size. Cholesterine, indeed, is insoluble in acid liquids, such as the urine; while it is soluble in soapy liquids, such as the bile. Such is solely the reason why the cholesterine is excreted by the biliary passages." *

Finally, in Dalton's "*Treatise on Human Physiology*," I find the following paragraph in which the subject of cholesterin is considered:

"CHOLESTERINE ($C_{26}H_{44}O$).—This is a crystallizable substance which resembles the fats in many respects, since it is destitute of nitrogen, readily inflammable, soluble in alcohol and ether, and entirely insoluble in water. It is not saponifiable, however, by contact with the alkalies, and is distinguished on this account from the ordinary fatty substances. It occurs, in a crystalline form, mixed with coloring matter, as an abundant ingredient in most biliary calculi, and is found also in different regions of the body, forming a part of various morbid deposits. We have met with it in the fluid of hydrocele, and in the interior of many encysted tumors. The crystals of cholesterine have the form of very thin, colorless, transparent, rhomboidal plates, portions of which are often cut out by lines of cleavage parallel to the sides of the crystal. They frequently occur deposited in layers, in which the outlines of the subjacent crystals show very distinctly through the substance of those which are placed above. Cholesterine is not formed in the liver, but originates in the substance of the brain

* "*Chimie appliquée à la physiologie et à la thérapeutique*," par M. le Docteur Mialhe, p. 191. Paris, 1856.

and nervous tissue, from which it may be extracted in large quantity by the action of alcohol. From these tissues it is absorbed by the blood, then conveyed to the liver, and discharged with the bile."*

The above extracts embrace all that I have been able to find bearing on the question of the function of cholesterin. The extracts from Mialhe and Dalton contain all that is said by them on this subject. Those from Carpenter and Lehmann contain only what bears on the function of this substance, the chemical details being omitted. Of the authors cited, Mialhe is the most extended on the subject and is almost the only one who adduces any arguments to support his views; but his opinions are biased by the purely chemical view which he takes of the subject, and are involved with the ideas with reference to plastic and calorific food, now rejected by many eminent physiologists, and which, I conceive, will be so little supported by future advances in science, that they will soon be universally discarded, in the exclusive sense in which they are received by him. Putting these hypotheses aside, examining the actual state of knowledge in regard to cholesterin, it is seen that its function, up to this time, has not been established. I shall now proceed to the facts which tend to support the statement I have made on this point.

Cholesterin exists in the blood, from which it may be extracted in a state of purity and estimated by the process which I have already indicated. Becquerel and Rodier have made analyses of the healthy human blood for this substance with the following results:

Venous blood of the male.....	0.09 pt. per 1,000
" " " female.....	0.09 " " "

I have made a quantitative analysis of three specimens of healthy human blood with the following results:

	Quantity of blood.	Cholesterin.	Proportion
	grains.	grains.	per 1,000 pts.
Venous blood from the arm ; male æt. 35	312.083	0.139	0.445
" " " (colored) æt. 22	187.843	0.123	0.658
" " " æt. 24	102.680	0.077	0.751

* "A Traité on Human Physiology," designed for the use of Students and Practitioners of Medicine. By John C. Dalton, Jr., M. D., Professor of Physiology and Microscopic Anatomy in the College of Physicians and Surgeons, New York, etc. Philadelphia, 1861, p. 189.

These three analyses were all carried on at the same time, each specimen being subjected to precisely the same process. The results show a wide range within the limits of health. The difference was not due to any variation relating to the digestive process, as the specimens were all drawn at the same time, and were taken from prisoners on Blackwell's Island, who were subjected to the same diet and ate at the same time. It will be seen by this table that I have obtained five to eight times more than is indicated by Becquerel and Rodier. I can explain this only by the fact that I operated on the whole blood, while they analyzed only the serum. Boudet states that it is necessary to make three to four copious bleedings and mix the serum in order to obtain a sufficient quantity for a satisfactory analysis. I have operated on about fifty grains of blood with success and have no doubt but that I should be able to extract the cholesterin in a crystalline form and estimate its quantity in fifteen or twenty grains. The purity of the extract can easily be demonstrated by a microscopic examination. I conclude, then, that a much larger quantity of cholesterin exists normally in the blood than has been supposed, and that its variations in different persons, within the limits of health, are considerable.

The next question which naturally arises is the origin of cholesterin. In examining the situations in which it is found it is seen that it exists in largest quantity in the substance of the brain and nerves. It is also found in the substance of the liver, probably in the bile which is contained in this organ, and in the crystalline lens, but with these exceptions it exists only in the nervous system and blood. Two views present themselves in regard to its origin. Cholesterin is deposited in the nervous matter from the blood or is formed in the brain and taken up by the blood. This is a question, however, which can be settled experimentally, by analyzing the blood for cholesterin as it goes to the brain by the carotid and as it comes from the brain by the internal jugular. Cholesterin being found also in the nerves, and, of course, a large quantity of nervous matter existing in the extremities, it is desirable at the same time to make an analysis of the venous blood from the general system.

With reference to this question the following experiment was made:

EXPERIMENT III.—A medium-sized dog, about six months old, fasting, was put under the influence of ether. The carotid and internal jugular were exposed on the left side and the animal allowed to come out from the effects of the anesthetic. Two hours after, he was again etherized and blood was taken from the following vessels in the order in which they are named: 1, internal jugular; 2, carotid; 3, vena cava; 4, hepatic veins; 5, hepatic artery; 6, portal vein. In the operation of drawing the blood from the abdominal vessels, immediately after opening the abdomen a ligature was applied to the vena cava and a little blood taken, which prevented the blood from the inferior extremities from mixing with the hepatic blood. The blood was then taken from the hepatic veins, a matter of some difficulty, as it is always more or less mingled with blood returning through the thoracic vena cava, and a ligature was applied to the hepatic artery and portal vein. The blood was then drawn from the hepatic artery and portal vein.* A quantity of bile was then taken from the gall-bladder, and a piece taken from the substance of the brain. These specimens were received into carefully weighed vessels and weighed; but as I failed to make a quantitative analysis, my process of extraction not having been perfected, it is unnecessary to enter into their details. They were then dried and pulverized, treated with ether, evaporated, the residue extracted with hot alcohol, allowed to evaporate spontaneously, and examined with magnifying powers of 70, 270, and 400 diameters successively. The residue of the bile and brain were found to consist of nearly pure cholesterin; but in all the other specimens, except that from the internal jugular, the appearance of cholesterin was doubtful. They all contained, with masses of ordinary fat, crystals of stercorin.† There were a few distinct

* The operation of collecting the blood from any particular vessel is by no means so easy as might at first be supposed. The greatest care is necessary in order to obtain it unmixed. This is particularly so in the case of the hepatic vein, the unmixed blood from which is exceedingly difficult to obtain. In drawing blood, the operation must be done as rapidly as possible to avoid the derangements of the circulation which arise from exposure of the vessels, pressure, etc. In taking blood going to and coming from a part, it must always be taken from the vein first; as ligating or compressing the artery would of course arrest the circulation. As the blood in the arterial system is not subject to the same changes in composition as the blood in the different veins, any specimen of arterial blood will represent the blood going to a part, unless, like the liver, it receives blood from the venous system. The collection of blood I have found the most difficult part of these investigations.

† Stercorin, or serolin, is a non-saponifiable fatty substance resembling cholesterin in many of its chemical properties, but fusing at a much lower temperature. It was discovered in the serum of the blood by Boudet about 1833. It crystallizes in the form of needles, which will be more particularly described when I treat of the extraction of this substance from the feces. As I have found it in great abundance in the feces and am disposed to doubt its existence as a natural constituent of the serum of the blood, I have called it stercorin, for reasons which will be more fully exposed farther on.

plates of cholesterin in the specimen from the internal jugular. The specimens were then treated with a solution of caustic potash and set aside. In two days part of the potash was removed with bibulous paper and portions of the precipitates taken out, placed upon slides, and examined microscopically with $\frac{1}{4}$ th and $\frac{1}{8}$ th inch objectives successively. The watch-glasses were then set aside, carefully protected from dust, and examined again ten days after, when they had become entirely dry. The following was the result of the examinations of the extracts of blood from the carotid, internal jugular, vena cava and the extract of the brain. The examination of the other specimens has nothing to do with the question now under consideration, and their description is deferred.

BLOOD FROM THE CAROTID ARTERY.—First examination, three days after the operation, discovered a large number of small crystals of stercorin and masses of fat; but after the most careful examination, prolonged for two hours, I failed to discover any crystals of cholesterin. The appearance is represented in Fig. 2.

The second examination, eleven days after, discovered a small quantity of cholesterin mixed with the matters noted in the first examination. This appearance is represented in Fig. 3.

SUBSTANCE OF THE BRAIN.—All the microscopic examinations of the extract from the brain showed crystals of cholesterin in large quantity. The crystals from the brain are described by Robin as being thinner and more elongated than those found in other situations.* This peculiarity I also noticed. The appearance is represented in Fig. 4.

BLOOD FROM THE INTERNAL JUGULAR.—In the first examination of the specimen from the internal jugular, after the blood had been treated with ether, the ether allowed to evaporate and the residue extracted with hot alcohol, well-marked plates of cholesterin were noted. At this time it could not be discovered in any of the other specimens of blood after the most careful and patient examination. After the caustic potash had been added, cholesterin was demonstrated in large quantity, with a few crystals of stercorin. The appearance is represented in Fig. 5, which was drawn eleven days after the blood was collected. Another examination was made on the following day, which showed, in addition to cholesterin, a considerable quantity of stercorin. (See Fig. 6.)

BLOOD FROM THE VENA CAVA.—The extract of the blood from the vena cava, examined eleven days after the blood was drawn, showed a large quantity of stercorin and a few crystals of cholesterin. Cholesterin was distinct but not very abundant. (See Fig. 7.)

These experiments, the first that I made on this subject, demonstrate the following facts: 1. That the brain contains a large quantity of cholesterin (which had, however, been previously established). 2. That the blood

* "*Traité de chimie anatomique*," Robin and Verdeil, tome iii., p. 57.

going to the brain contains a small quantity of cholesterin, while the blood coming from the brain contains a large quantity. 3. That the blood coming from the lower extremities and pelvic organs contains more cholesterin than the blood carried to them by the arterial system.

It was only necessary to confirm these statements by further investigation, to be enabled to deduce from them the following important conclusions: That cholesterin is formed in some of the tissues of the body; and, judging from the fact that the nervous tissue is the only one in which it is found and that the blood gains it in its passage through the great nervous centre, it is formed in great part by the nervous system. After the first experiment, which almost confirmed the supposition with which I had started, I directed my attention to the perfection of a process by which I might make an accurate quantitative analysis of the blood for cholesterin, so as to be able to state positively that it gained cholesterin in its passage through certain organs, and furthermore to determine the amount of increase. After a number of experiments I fixed upon the process which I have minutely described in the first part of this article, and made the following experiments for the purpose of ascertaining the quantity of cholesterin produced in the brain:

EXPERIMENT IV.—A medium-sized adult dog was put under the influence of ether and the carotid artery, internal jugular and femoral veins exposed. Specimens of blood were drawn, first from the internal jugular, next from the carotid, and last, from the femoral vein. These specimens were received into carefully weighed vessels and weighed.

They were then analyzed for cholesterin by the process already described, and the following results obtained:

	Quantity of blood. grains.	Cholesterin. grains.	Cholesterin per 1,000 pts.
Carotid.....	179.462	0.139	0.774
Internal jugular.....	134.780	0.108	0.801
Femoral vein.....	133.886	0.108	0.806

Percentage of increase in blood from the jugular over the arterial blood..... 3.488

Percentage of increase of blood from the femoral vein..... 4.134

This experiment shows an increase in the quantity of cholesterin in the blood during its passage through the brain and an increase, even a little greater, in the blood

passing through the vessels of the posterior extremity. To facilitate the operation, however, the animal was brought completely under the influence of ether, which, from its action on the brain, would not improbably produce some temporary disturbance in the nutrition of that organ and consequently interfere with the experiment. For the purpose of avoiding this difficulty I performed the following experiments without administering an anesthetic:

EXPERIMENT V.—A small young dog was secured to the operating table and the internal jugular and the carotid exposed on the right side. Blood was taken, first from the jugular and afterward from the carotid. The femoral vein on the same side was then exposed and a specimen of blood taken from that vessel. The animal was very quiet under the operation, though no anesthetic was used, so that the blood was drawn without any difficulty and without the slightest admixture.

The three specimens were analyzed for cholesterin with the following results:

	Quantity of blood grains.	Cholesterin. grains.	Cholesterin per 1,000 pts.
Carotid.....	143.625	0.679	0.967
Internal jugular.....	29.956	0.046	1.545
Femoral vein.....	45.035	0.046	1.028

Percentage of increase in blood from the jugular over arterial blood.....	59.772
Percentage of increase of blood from the femoral vein.....	6.308

EXPERIMENT VI.—A large and powerful dog was secured to the operating table and the carotid and internal jugular exposed. Specimens of blood were taken from these vessels, first from the jugular, carefully weighed and analyzed for cholesterin in the usual way. The following results were obtained:

	Quantity of blood. grains.	Cholesterin. grains.	Proportion in 1,000 pts.
Carotid.....	140.847	0.108	0.768
Internal jugular.....	97.811	0.092	0.947
Percentage of increase in passing through the brain.....	23.307		

Experiment V. shows a very considerable increase in the quantity of cholesterin in the blood passing through the brain, while it is comparatively slight in the blood of the femoral vein. The proportion of cholesterin is also large in the arterial blood as compared with other observations.

Experiment VI. shows but a slight difference in the quantity of cholesterin in the arterial blood in the two animals; the proportion in the animal that was etherized being 0.774 pts. per 1,000, and in the animal that was not ether-

ized 0.768 per 1,000, the difference being but 0.006; but, as I had suspected, the ether had an influence on the quantity of cholesterin absorbed by the blood in its passage through the brain. In the first instance the increase was but 3.488 per cent., while in the latter it was 23.307. Unfortunately the blood was not taken from the femoral vein. I intended to take blood from the abdominal organs, but after opening the abdomen the struggles of the animal were so violent that this was impossible, and he was killed.

What are the natural conclusions, from the preceding experiments, in regard to the origin of cholesterin in the economy? It has been found that the brain and nerves contain a large quantity of this substance, which is found in none other of the tissues of the body. The preceding experiments, especially Experiments V. and VI., show that the blood which comes from the brain contains a much larger quantity of cholesterin than the blood which goes to this organ.

The conclusion is, then, that cholesterin is produced in the brain and thence absorbed by the blood.

But the brain is not the only part where cholesterin is produced. It will be seen by Experiment IV. that there is 4.134 per cent., and in Experiment V., 6.308 per cent. of increase in cholesterin in the passage of the blood through the inferior extremities, and probably about the same in other parts of the muscular system. In examining these tissues chemically, I find that the muscles contain no cholesterin, but that it is abundant in the nerves; and as it is found that the proportion of cholesterin is immensely increased in the passage of the blood through the great centre of the nervous system, taken, as the specimens examined were, from the internal jugular, which collects the blood from the brain and very little from the muscular system, it is rendered almost certain, that in the general venous system, the cholesterin which the blood contains is produced in the substance of the nerves.

If this is true, and if, as I hope to show, cholesterin is a product of the destructive assimilation of nervous tissue, its production would be proportionate to the activity of the nutrition of the nerves; and anything which interfered to any great extent with their nutrition would diminish the quantity of cholesterin produced. In the

production of urea by the general system, which is an analogous process, muscular activity increases the quantity, and inaction diminishes it, on account of the effect upon nutrition. In cases of paralysis there is a diminution of the nutritive forces in the parts affected, especially of the nervous system, which, after a time, becomes so disorganized, that although the cause of the paralysis be removed, the nerves can not resume their functions. It is true that this exists to a certain extent in the muscles; but it is by no means so marked as it is in the nerves. We should be able, then, to confirm the observations on animals by examining the blood in cases of paralysis; when we should find a very marked difference in the quantity of cholesterin between the venous blood coming from the paralyzed parts and that from other parts of the body. With this in view I made analyses of the blood from both arms in three cases of hemiplegia, which seemed to me most suitable for such a comparison:

CASE I.—Sarah Rumsby, æt. 47, affected with hemiplegia of the left side. Two years ago she was taken with apoplexy and was insensible for three days. When she recovered consciousness she found herself paralyzed on the left side. Said she had epilepsy four or five years before the attack of apoplexy. Now she has entire paralysis of motion on the affected side, with the exception of some slight power over the fingers, but sensation is perfect. The speech is not affected. The general health is good.

CASE II.—Anna Wilson, æt. 23, Irish, affected with hemiplegia of the right side. Four months ago she was taken with apoplexy, from which she recovered in one day with loss of motion and sensation on the right side. She is now improving and can use the right arm slightly. The leg is not so much improved because she will make no effort to use it.

CASE III.—Honora Sullivan, Irish, æt. 40, affected with hemiplegia of the right side. About six months ago she was taken with apoplexy and recovered consciousness the next day, with paralysis. The leg was less affected than the arm, from the first. The cause was supposed by Dr. Flint, the attending physician, to be due to an embolus. Her condition is now about the same as regards the arm, but the leg has somewhat improved.

These cases all occurred at the Blackwell's Island Hospital. The treatment in all consisted of good diet, frictions, passive motion and use of the paralyzed members as much as possible.

A small quantity of blood was drawn from both arms in these three cases. It was drawn from the paralyzed

side, in each instance, with great difficulty, and but a small quantity could be obtained.

The specimens were all examined for cholesterin, with the following results:

TABLE OF QUANTITY OF CHOLESTERIN IN BLOOD OF PARALYZED AND SOUND SIDES IN THREE CASES OF HEMIPLEGIA

		Blood.	Cholesterin.	Cholesterin per 1,000.
		grains.	grains.	
Case I.	Paralyzed side....	55.458	The watch-glass contained 0.031 grain of a substance, but the most careful examination failed to show a single crystal of cholesterin.
"	Sound side.....	128.407	0.062.	0.481.
Case II.	Paralyzed side....	18.381	Same as Case I.
"	Sound side.....	66.396	0.062	0.808.
Case III.	Paralyzed side....	21.842	Same as Case I.
"	Sound side.....	52.261	0.031	0.579.

The result of these examinations is very interesting: not a single crystal of cholesterin was found in any of the three specimens of blood from the paralyzed side, while about the normal quantity was found in the blood from the sound side. As the nutrition of other tissues is interfered with in paralysis, it is impossible to say positively, from these observations alone, that cholesterin is produced in the nervous system only. But the nutrition of the nerves is undoubtedly most affected; and this observation, taken in connection with the preceding experiments on animals, seems to settle where cholesterin is produced.

I may extend my first conclusion, then, and state that cholesterin is produced in the substance of the nervous system.

Before entering upon the character of cholesterin and inquiring whether it is an excrementitious or recrementitious product, I shall endeavor to follow it out in the system and ascertain if there is any organ which separates it from the blood. In pursuing this question, the method will be adopted that has been employed in investigating its origin; that is, analyzing the blood as it goes to and comes from certain organs. The organ which one would

be led first to examine is the liver, as it is the only gland the product of which contains cholesterin, which, if not manufactured in the gland itself, must be separated from the blood.

In the first series of experiments which I performed on this subject, I endeavored to show on the same animal the origin of cholesterin in certain parts and its removal from the body. In these experiments—in which the results were approximative, as I had not succeeded in extracting cholesterin perfectly pure—I began with the arterial blood, examining it as it went into the brain by the carotid, analyzing the substance of the brain; then analyzing the blood as it came out of the brain by the internal jugular; examining the blood as it went into the liver by the hepatic artery and portal vein; examining the secretion of the liver; then the blood as it came out of the liver by the hepatic vein; examining also the blood of the vena cava in the abdomen. The analyses of the blood from the carotid, internal jugular, and vena cava have already been referred to, in treating of the origin of cholesterin. It will be remembered that there was a large quantity of this substance in the internal jugular, and but a small quantity in the carotid, showing that it was formed in the brain. I now give the conclusion of those observations, which bears upon the separation of cholesterin from the blood.

EXPERIMENT VII.—Specimens of blood were taken from the hepatic artery, portal vein and hepatic vein, and a small quantity of bile from the gall-bladder. These specimens were treated in the manner already indicated in Experiment III.; i. e., evaporated and pulverized, extracted with ether, the ether evaporated, and the residue extracted with boiling alcohol, this evaporated, a solution of caustic potash added and then subjected to a microscopic examination.

BLOOD FROM THE PORTAL VEIN.—Microscopic examination of the extract from the portal vein showed quite a number of crystals of cholesterin, which are represented in Fig. 8. These were observed after the fluid had nearly evaporated.

BLOOD FROM THE HEPATIC ARTERY.—Microscopic examination of the extract from the hepatic artery, made after the fluid had nearly evaporated, showed a considerable quantity of cholesterin, more than was observed in the preceding specimen. (See Fig. 9.) There were also observed a few crystals of stercorin, represented in Fig. 10.

BLOOD FROM THE HEPATIC VEIN.—The first examination of the extract from the hepatic vein, which was made just before the

potash was added, showed a number of fatty masses with some crystals of stercorin. The solution of potash was then added, and two days after, another careful examination was made, discovering nothing but fatty globules and granules. (See Fig. 11.) The watch-glass was then set aside and was examined eleven days after, when the fluid had entirely evaporated. At this examination a few crystals of cholesterin were observed for the first time. (See Fig. 12.) There were also a number of crystals of margaric and of stearic acid.

BILE.—All the examinations of the extract from the bile showed cholesterin; the precipitate consisted, indeed, of this substance in a nearly pure state. Fig. 13 represents some of the crystals which were observed in this specimen.

Considering this series of experiments in connection with the first observations on the carotid and internal jugular, while the one series demonstrates pretty conclusively that cholesterin is formed in the brain, the other shows that it disappears, in a measure, from the blood in its passage through the liver and is found in the bile. In other words, it is formed in the nervous tissue and prevented from accumulating in the blood by its excretion by the liver. This suggests an interesting series of inquiries; and this fact, if substantiated, would be as important to the pathologist as to the physiologist. But in order to settle this important question, it is necessary to do something more than make an approximate estimate of the quantity of cholesterin removed from the blood by the liver. The quantity which is thus removed in the passage of the blood through this organ should be estimated, if possible, as closely as the quantity which the blood gains in its passage through the brain. But this estimate is more difficult. The operation for obtaining the blood, in the first place, is much more serious than that for obtaining blood from the carotid and internal jugular. It is very difficult to obtain the unmixed blood from the hepatic vein; and the exposure of the liver, if prolonged, must interfere with its eliminative function, in the same way that exposure of the kidneys arrests in a few moments the flow from the ureter. It is probable, however, that the administration of ether does not interfere with the elimination of cholesterin by the liver as it does apparently with its formation in the brain. Anesthetics have a peculiar and special action on the brain, but they do not interfere with the functions of vegetative life, like secretion or excretion; and there-

fore they would not interfere with the depurative function of the liver. It is fortunate that this is the case, for the operation of taking blood from the abdominal vessels is immensely increased in difficulty by the struggles of an animal not under the influence of an anesthetic, so much so, indeed, that I failed entirely in obtaining any blood from one animal (the one used in Experiment VI.), which was not etherized. It was a very powerful dog, and his struggles were so violent that it was impossible to collect the blood accurately from the abdominal vessels and the attempt was abandoned. With the view of settling the question of the disappearance of a portion of the cholesterolin of the blood in its passage through the liver, by an accurate quantitative analysis, I repeated the operation for drawing blood from the vessels which go into and emerge from the liver. In my first trial the blood was drawn so unsatisfactorily and the operation was so prolonged, that I did not think it worth while to complete the analysis and abandoned the experiment. In the following one I was more successful:

EXPERIMENT VIII.—A good-sized bitch (pregnant) was brought completely under the influence of ether, the abdomen laid freely open, and blood drawn first from the hepatic vein, and next from the portal vein. The taking of the blood was entirely satisfactory, the operation being done rapidly and the blood collected without any admixture. A specimen of blood was then taken from the carotid to represent the blood from the hepatic artery.

The three specimens of blood were then examined in the usual way for cholesterolin, with the following results:

	Quantity of blood, grains.	Cholesterolin, grains.	Cholesterolin in 1,000 pts.
Arterial blood.....	159.537	0.200	1.257
Portal vein.....	168.257	0.170	1.009
Hepatic vein.....	79.848	0.077	0.964
Percentage of loss in arterial blood in its passage through the liver.....			23.309
Percentage of loss in blood of the portal vein.....			4.460

This experiment proves positively what there was good ground for supposing from Experiment VII.; namely, that cholesterolin is separated from the blood by the liver; and here I may note, in passing, a striking coincidence between the analysis in Experiment VI., when the blood was studied in its passage through the brain, and the one just mentioned, when the blood was studied in its passage

through the liver. The gain of the arterial blood in cholesterin in passing through the brain was 23.307 per cent., and the loss of this substance in passing through the liver is 23.309 per cent. There must be, of course, the same quantity separated by the liver that was formed by the nervous system, it being formed, indeed, only to be separated by this organ, its formation being continuous, and its removal necessarily the same, in order to prevent its accumulation in the circulating fluid. The almost exact coincidence between these two quantities, in specimens taken from different animals, though not at all necessary to prove the fact just mentioned, is still very striking.

It is shown by Experiment VIII. that the portal blood, as it goes into the liver, contains but a small percentage of cholesterin over the blood of the hepatic vein, while the percentage in the arterial blood is large. The arterial blood is the mixed blood of the entire system; and as it probably passes through no organ before it gets to the liver, which diminishes its cholesterin, it contains a quantity of this substance which must be removed. The portal blood, coming from a limited part of the system, contains less of this substance, though it gives up a certain quantity. In the circulation in the liver, the portal system largely predominates, and is necessary to other important functions of this organ, such as the production of glycogen. Soon after the portal vein enters the liver, its blood becomes mixed with that from the hepatic artery,* and from this mixture cholesterin is separated. It is only necessary that blood, containing a certain quantity of cholesterin, should come in contact with the bile-secreting cells, for this substance to be separated. The fact that it is eliminated by the liver is proved with much less difficulty than that it is formed in the nervous system. In fact, its presence in the bile, the necessity for its constant removal from the blood, which is consequent on its constant formation and absorption by this fluid, are almost

* According to Robin, the branches of the hepatic artery are distributed almost entirely in the interlobular plexuses and on the walls of the hepatic duct and portal vein and do not find their way into the substance of the lobules.—“Dictionnaire de médecine, de chirurgie, de pharmacie, des sciences accessoires et de l'art vétérinaire,” P. H. Nysten ; “onzième édition revue et corrigé.” Par E. Littré et Ch. Robin. Paris, 1858. Article “Foie.”

sufficient in themselves to warrant the conclusion that it is removed by the liver. This, however, is put beyond a doubt by the preceding analysis of the blood going to and coming from this organ.

Another link, then, is added to the chain of facts which make up the history of cholesterin. The first is that—

Cholesterin is formed in the brain and nervous system and is absorbed by the blood.

The second, which has just been proved, is that—

Cholesterin, formed in these situations and absorbed by the blood, is separated from the blood in its passage through the liver.

The next question, in following out this line of inquiry, is, what becomes of the cholesterin which is separated from the blood? This question is very easily answered, and necessitates only an examination of one of the products of the liver, the bile.

BILE.—In the few remarks with which I prefaced this article, I spoke of the various opinions which are held by physiologists with reference to the function of the bile; some regarding it as purely excrementitious, others placing it among the recrementitious fluids. I detailed experiments which led me to think that it had two distinct functions: one, which is recrementitious and is probably concerned in digestion to an important degree, but which it is not designed to take up in this connection; the other, which is excrementitious, and which is necessarily taken up in a discussion of the important substance now under consideration. A glance at the composition of the bile will show that it is an exceedingly complex fluid; and physiological investigations into the destination of certain of its ingredients, by Bidder and Schmidt, Dalton and others, have shown that they are not discharged from the body, but reabsorbed by the blood; though the failure to detect them in the portal blood by the appropriate tests shows that in this reabsorption they probably undergo some alteration.* These substances, which have heretofore been considered as the most important ingredients of the bile,

* For a very complete account of the bile, with original investigations into the destination of the biliary salts, the reader is referred to an article published by Prof. John C. Dalton, Jr., in the "American Journal of the Medical Sciences," October, 1857, and the chapter on bile in Dalton's "Physiology."

though their function is obscure, are the glycocholate and taurocholate of soda, discovered by Strecker in the bile of the ox, in 1848. The following is the composition of the bile given in Dalton's "Physiology," which is "based on the calculations of Berzelius, Frerichs and Lehmann." *

COMPOSITION OF OX BILE	
Water.....	880.00
Glycocholate of soda.....	} 90.00
Taurocholate of soda.....	
Biliverdin.....	} 13.42
Fats	
Oleates, margarates and stearates of soda and potassa..	
Cholesterin.....	} 15.24
Chloride of sodium.....	
Phosphate of soda.....	
Phosphate of lime.....	
Phosphate of magnesia.....	
Carbonates of soda and potassa.....	} 1.34
Mucus of the gall-bladder.....	
	1,000.00

Of the above ingredients of the bile, are biliverdin, which is simply a coloring matter; fats, with oleates, margarates and stearates, which, with the biliary salts, are said to hold the cholesterin in solution; chloride of sodium, present in all the animal fluids; phosphates and carbonates, which are simple excreted and are also ingredients of the urine; leaving, as the most important constituents, of which the function is least understood, the biliary salts and cholesterin. The biliary salts are probably recrementitious; but cholesterin is one of the products of the waste of the system. The bile, then, presents the combined character, so far as its chemical composition is concerned, of a secretion and of an excretion. I may now contrast these two properties and see what this fluid has in common with the secretions and how it obeys the laws which regulate the excretions. In doing this I shall first contrast some of the important distinctions between these two classes of products.

Secretions are characterized by certain constituents which are formed in the substance of the gland and are found in no other situation. Such is the pancreatin of the pancreatic juice, the pepsin of the gastric juice, the

* Dalton's "Physiology," second edition, p. 158.

ptyalin of the saliva, and, I may add, the glycocholate and the taurocholate of soda of the bile.

These substances first make their appearance in the substance of the gland itself; they do not preëxist in the blood; they are discharged from the gland for a special purpose, and when there is no necessity for their action, the discharge does not take place. Illustrations of this are to be found in the digestive fluids, which are true secretions; poured out only when this function is called into action by the ingestion of food, and not discharged from the body, but their elements taken up again by the blood when their function has been accomplished. Thus the gastric and pancreatic fluids are never secreted until food is taken into the alimentary canal, and are reabsorbed with the digested matters.

The flow of the secretions is intermittent, and the gland, during the period of repose, manufactures the elements of the secretion, which are washed out at the duct when the appropriate stimulus (of food, for example) causes a determination of blood to the organ. The gland manufactures the elements of the secretion, and the blood furnishes the menstruum, the water, by means of which they are dissolved and emptied into the duct. When the pancreas of an animal is exposed during the intervals of digestion, it is pale and bloodless; no fluid flows from the duct; but the elements of the pancreatic juice are, nevertheless, in the gland; for they may be dissolved out from the gland, and an artificial pancreatic juice results which will have all the reactions and digestive properties of the natural secretion. But if the pancreas of an animal is exposed during digestion, the gland is turgid with blood; the secretion flows from the duct, and the products of the gland are being washed out by the blood—a process which is imitated when they are dissolved out by maceration in water. The late brilliant experiments of Bernard have shown that the function of the glands is regulated by the nervous system, and that faradization of certain nerves, by which the nervous force is imitated, will cause a determination of blood to the organ and induce secretion, while stimulation of other nerves will contract the vessels and arrest secretion.

The substances which characterize the secretions, as

they are manufactured in the glands and do not preëxist in the blood, do not accumulate in the blood when the gland is removed or its functions are interfered with.

The distinctive characters of the secretions, in fact, may be summed up thus:

Their elements first appear in the glands and do not preëxist in the blood. They are not discharged from the body, with the exception of the milk, which is destined for the nourishment of the child. Their flow is intermittent. They are destined to assist in some of the nutritive functions of the body.

Excretions, of which the urine may be taken as a type, have entirely different characteristics:

Excrementitious substances do not first make their appearance in the organs which separate them, but are produced in the general system.

They preëxist in the blood, having been absorbed by this fluid from the parts of the system in which they are formed, are carried to particular organs and are separated from the blood for the sole purpose of being expelled from the body. An illustration of this is to be found in urea, which has been detected in the blood and urine and some of the tissues of the body. This substance, one of the most important excrementitious products, is absorbed by the blood from certain parts of the system, carried to the kidneys, there separated from the blood and discharged from the body. Although the gastric and pancreatic fluids, and all the secretions proper, are reabsorbed with the food after they have acted upon it, urea may remain any length of time in the bladder, but it is never absorbed.

The flow of the excretions is constant. No period of repose is necessary for the gland to manufacture their elements, as they all preëxist in the blood. Nutrition is constant, and destructive assimilation, or waste, which necessitates nutrition or repair, is likewise constant. The blood supplies all the wants of the system and receives all the products of its decay. As the blood is continually being impoverished, it must be regenerated from without; and this is done by food, which is prepared for absorption by digestion. The secreted fluids are chiefly concerned in digestion; and as this is an occasional process, the secretions are intermittent. But waste is continually going

on and excrementitious substances are continually forming; and while the necessity for the secretions is occasional, the necessity for the excretions is constant. Though the actual discharge of the latter from the body is occasional, they are constantly being separated from the blood, and accumulate in receptacles, whence they are discharged at appropriate intervals. No such receptacles exist for the secretions proper, except in the instance of the milk, which accumulates in the ducts of the mammary gland and is the only secretion which is discharged from the body.

If the secreting glands take on an excretory function, as is an occasional pathological occurrence, their flow becomes continuous. An example of this is the occasional separation of urea from the blood by the gastric tubules. When the kidneys become so affected by disease as to be unable to separate the urea from the system, the accumulation of this excretion in the blood frequently induces other organs to attempt its removal. The gastric tubules take on this function and produce a fluid which contains urea. The gastric juice, if I may now so term it, is no longer a secretion but an excretion; and its flow is no longer intermittent and dependent upon the stimulus of food introduced into the stomach, but is constant, and continues until the irritation caused by the decomposing urea in the stomach induces an inflammation which prevents further secretion. This is an example of an intermittent secretion, characterized by a substance manufactured in the gland and not preëxisting in the blood, changed into a constant excretion, characterized by a substance which is not manufactured in the gland but preëxists in the blood.

The substances which characterize the excretions accumulate in the blood when the organ which eliminates them is removed or its functions are interfered with. It is this fact which led to a knowledge that urea preëxisted in the blood. It was detected in that fluid when it had accumulated in animals from which the kidneys had been removed, and in cases of Bright's disease of the kidneys, before chemical processes were sufficiently delicate to detect it in healthy blood, when the quantity is kept down by its constant elimination by the kidneys.

The characters of the excretions, then, are entirely opposite to those of the secretions.

Their elements preëxist in the blood and are not manufactured in the substance of the organs which eliminate them. Their flow is constant. They are separated from the blood merely to be discharged from the body and are not destined to assist in any of the nutritive functions.

Having contrasted the secretions and the excretions, I shall now examine the bile and note what are the characters which it has in common with either or both of these products.

The bile is characterized by two kinds of constituents: One of them, the glycocholate and the taurocholate of soda, manufactured in the liver, found in no other fluid than the bile, does not preëxist in the blood, and associates the bile with the secretions. The other, the cholesterin, preëxists in the blood and is simply separated from it by the liver, giving the bile one of the characters of an excretion.

The biliary salts (the glycocholate and taurocholate of soda) are discharged into the intestinal canal for a special purpose; and this discharge takes place at the beginning of the digestive act. If the liver and gall-bladder of a dog which has not taken food is exposed, the gall-bladder will be found distended with bile; but if these organs are examined when digestion is going on, the gall-bladder will be found nearly empty. It is true that after prolonged fasting the bile is discharged into the alimentary canal, but it must be remembered that it contains another ingredient, cholesterin, which must be discharged from the body, as will appear presently. The biliary salts are not discharged from the body. Dr. Dalton has shown that the substances extracted from the contents of the large intestine by evaporation, extraction of the residue with alcohol and precipitation with ether, will not react with Pettenkofer's test, which is a very delicate test for the biliary salts. I have treated the feces of the human subject in the same way with the same result. These salts, therefore, are not discharged from the body unchanged. The next question to determine is whether they are discharged from the body in a modified form. They contain a certain quantity of sulphur, of which, as has been shown by Bidder and Schmidt, only one-fifteenth part of the entire quantity which enters the intestine with the bile can be detected in the feces. As sulphur is an elementary sub-

stance, it can not be decomposed; and the biliary salts, in their passage down the alimentary canal, must be absorbed. It is true that these salts can not be detected in the blood coming from the intestines, but we can not detect the pancreatin of the pancreatic juice, the pepsin or the acid of the gastric juice in the portal blood, yet these are absorbed by the mucous membrane of the intestinal tube, changed by their union with the matters they have digested. It is probable that an analogous change takes place in the glycocholate and taurocholate of soda, which prevents them from being detected in the blood by the ordinary tests. These facts, also, place the bile among the secretions.

On the other hand, cholesterin preëxists in the blood, having been absorbed by this fluid from certain parts of the system, is carried to the liver and there separated for the sole purpose of being discharged from the body. The same general remarks apply to this substance as to urea. This places the bile among the excretions.

The flow of the secretions is intermittent. This is not absolutely true of the bile, but the discharge of this fluid is remittent. Dr. Dalton * has reported a series of interesting experiments upon an animal with a duodenal fistula. In this observation ten grains of dry biliary matter were discharged into the duodenum of a dog weighing thirty-six and a half pounds, immediately after feeding. At the end of the first hour it had fallen to four grains; it continued at three and a half to four and a half grains up to the eighteenth hour, when the quantity was inappreciable; at the twenty-first hour it was one grain; the twenty-fourth, three and a quarter grains; and the twenty-fifth, three grains. The fluid was drawn for fifteen minutes each time, evaporated to dryness, extracted with absolute alcohol, precipitated with ether, the ether precipitate dried and weighed as representing the quantity of biliary matter present. These experiments apply to the time when the bile is discharged into the intestine; but as most animals have a gall-bladder, which collects the bile as it is secreted, it does not show when this fluid is formed by the liver. Schwann, Bidder and Schmidt, Arnold, Kölliker and Mül-

* Dalton, "Constitution and Physiology of the Bile." *Loc. cit.*

ler, have made experiments bearing upon the latter point, by ligating the ductus communis choledochus and making a fistula into the fundus of the gall-bladder. The experiments of these observers vary somewhat in regard to the time when the secretion of the bile is at its maximum. In the animal already referred to, in which a fistula was made into the fundus of the gall-bladder, the bile was collected for thirty minutes immediately after feeding, one hour after, and then at intervals of two hours during the remainder of the twenty-four hours. The specimens of bile thus collected were carefully weighed, evaporated to dryness and the proportion of dry residue taken. The following table shows the results of these observations, which were made twelve days after the operation, when the animal, which weighed originally twelve pounds, had lost two pounds. His appetite was ravenous at the time of the experiment.

TABLE OF THE VARIATIONS OF THE BILE IN THE TWENTY-FOUR HOURS. At each observation the bile was drawn for precisely thirty minutes. Dog with a fistula into the gall-bladder. Weight ten pounds.

TIME AFTER FEEDING.	Fresh bile.	Dried bile.	Percentage of dry residue.
	grains.	grains.	
Immediately.....	8.103	0.370	4.566
One hour.....	20.527	0.586	2.854
Two hours.....	35.760	1.080	3.023
Four hours.....	38.939	1.404	3.605
Six hours.....	22.209	0.987	4.450
Eight hours.....	36.577	1.327	3.628
Ten hours.....	24.447	0.833	3.407
Twelve hours.....	5.710	6.247	4.325
Fourteen hours.....	5.000	0.170	3.400
Sixteen hours.....	8.643	0.309	3.575
Eighteen hours.....	9.970	0.277	2.778
Twenty hours.....	4.769	0.170	3.565
Twenty-two hours.....	7.578	0.293	3.866
Twenty-four hours.....	15.001	0.885	5.233

This table shows a regular increase in the quantity of bile discharged from the fistula from the time of feeding up to four hours after. It diminished at the sixth hour, rose again at the eighth hour, but then gradually diminished to the fourteenth hour. There was then a slight increase the sixteenth and eighteenth hours, and the twen-

tieth hour it fell to its minimum. It then increased slightly the twenty-second hour, and mounted considerably the twenty-fourth hour, when the observations were concluded. Disregarding slight variations in the quantity, which might be accidental, it may be stated in general terms that the maximum flow of bile from the liver is from the second to the eighth hour after feeding, during which time it is about stationary. In this experiment it was at its minimum the twentieth hour after feeding. This observation agrees with those of Bidder and Schmidt as regards the time when the bile begins to increase in quantity; but these observers state that it is at its maximum from the twelfth to the fifteenth hour. This, however, is not material to the question now under consideration. I wished to establish the fact that the quantity of bile secreted varied considerably during the various stages of the digestive act; a character which approximates it to other secretions. The flow of the bile is not intermittent, because it contains a substance which is excrementitious; but it is remittent, having a definite relation to the digestive act, because it contains substances which are recrementitious and are in some way connected with the process of digestion.

The continuous though remittent flow of the bile allies it with the excretions. There is no time, in health, when the bile is not separated from the blood. In animals that go through the process of hibernation, the bile continues to be secreted, though no food is taken into the alimentary canal. Nutrition, though much diminished in activity, goes on during this state, and the urea and cholesterol must be separated from the blood. The formation of the bile and urine, therefore, is not interrupted. Bile is secreted also in the foetus, before any nourishment is taken into the alimentary canal, when none of the other digestive fluids are formed. This character it has in common with the urine, and this places it among the excretions.

The elements of secretion never accumulate in the system when the secretion is interfered with; while the elements of excretion do accumulate in the blood in such cases and produce certain toxic effects. Experimenters have often analyzed the blood for the biliary salts in cases of serious disease of the liver, marked by symptoms of bile-poisoning, regarding these as the only important elements

of the bile; but they have never been detected. I have made no observations on this point, for the fact that the glycocholate and taurocholate of soda do not accumulate in the blood in diseases of the liver has long been settled. This stamps these substances as products of secretion; but we shall see when some of the pathological conditions of the cholesterin are taken up, that this substance does accumulate in the blood when the functions of the liver are seriously interfered with, which marks it as a product of excretion.

It seems to me that enough has been said in regard to the function of the bile to convince the reader that this complex fluid has two important ingredients which have two separate functions.

First.—It contains the glycocholate and taurocholate of soda, which are not found in the blood, are manufactured in the liver, are discharged mainly at a certain stage of the digestive process, are destined to assist in some of the nutritive processes, are not discharged from the body and, in fine, are products of secretion.

Second.—It contains cholesterin, which is found in the blood, is merely separated from it by the liver and not manufactured in this organ, is not destined to assist in any of the nutritive processes but is merely separated to be discharged from the body, and is a product of excretion.

These two propositions, especially the second, being established, it becomes necessary now to follow out cholesterin after it has been discharged from the liver into the small intestine. If it is discharged from the body it must be by the rectum; and to complete the history of cholesterin it becomes necessary to study the feces.

FECES.—It is not my object to consider all the effete matters which go to make up the feces, although it must be acknowledged that information on this subject is very limited. Following cholesterin in its passage down the alimentary canal has opened a new subject for investigation, to which it will be impossible to do entire justice in this paper. There is a field for a long series of investigations into this part of our subject, which I hope to be able to cultivate to some extent in the future and to add something to the history of the substance I have been considering. At present I shall endeavor only to demon-

strate the fact that cholesterin, in a modified form, is discharged with the feces, and not attempt to treat of the conditions which modify the excretion of this substance (upon which as yet I have no data), which are of great importance to the practical physician.

It is stated by some of the most reliable authors on physiology and physiological chemistry that cholesterin is found in the fecal matters. Robin and Verdeil say, "*Ce principe immédiat se trouve à l'état normal dans le sang, la bile, le foie, le cerveau, les nerfs, le cristaillon et les matières fécales.*" Many other authors refer to it as found in the feces, and it was with that belief, that, in the experiments which form the basis of this article, I deferred my analyses of the feces till I had completed the observations on the blood, and then analyzed them, satisfied that I should find cholesterin, with the view to determine the variations, etc., in its quantity. When, after a careful and prolonged examination of many specimens of feces, I was unable to extract any cholesterin, I endeavored to ascertain what observer had established its presence. Though it is mentioned by so many as present in fecal matter, I could find no mention of any one who had established this point; and in some of the analyses of Simon, I found that he had noted its absence in certain specimens of feces. I found also that Marcet, who published some elaborate analyses of the feces in the "*Philosophical Transactions,*" in 1854 and 1857, noted the absence of cholesterin in the normal feces of the human subject. It has already been seen how conclusively the experiments on the blood from various parts of the system point to the excrementitious character of cholesterin, showing, even, in what part of the system it is found and where it is eliminated; but it is undoubtedly one of the most important characters of an excretion that it should be discharged from the body, and I was unable for a time to convince myself that it was discharged. After evaporating the feces to dryness, pulverizing, extracting thoroughly with ether, decolorizing with animal charcoal, evaporating the ether and extracting the residue with boiling alcohol, I allowed the alcohol to evaporate, added a solution of caustic potash, and kept the mixture at a temperature near the boiling point for three and a quarter hours. The potash was then carefully

washed away on a filter, the residue redissolved in ether and extracted with hot alcohol as before, and the alcoholic extract set aside to evaporate. A number of days passed without any sign of crystallization. The residue was, of course, non-saponifiable; but it differed from cholesterin by being melted at a much lower temperature, though it presented the red color with sulphuric acid which is said to be characteristic of the latter substance. It was examined carefully with the microscope daily; and after five or six days, to my great satisfaction, crystals began to appear; but they were at first so indistinct that their form could not be clearly made out. These crystals, however, increased in size and number, and in a short time presented the characteristics of serolin. In about ten days the whole mass had crystallized, making one of the most superb exhibitions of crystals that could be imagined. Serolin crystallizes in the form of delicate transparent needles, which have a beauty under the microscope which could be but poorly imitated by the most delicate steel plate engraving. This substance, from its being found in such large quantity in the feces, I have spoken of as stercorin.

Before taking up the changes which cholesterin undergoes in its passage down the alimentary canal, I shall say a few words in regard to stercorin.

STERCORIN

Stercorin has already been referred to and delineated in the analyses of various specimens of blood for cholesterin. It was observed by Boudet and described by him under the name of séroline, in an article published in the "*Annales de chimie et de physique*," in 1833, as a principle found in the serum of the blood. Up to the present time, this is the only situation in which it has been found, and here in such an excessively minute quantity that enough has never been obtained for ultimate chemical analysis. In regard to its function nothing whatever has been known. Robin thus speaks of it: "On ne sait pas comment se forme la séroline, ni quel est son rôle physiologique." *

* Robin and Verdeil, "*Chimie anatomique et physiologique*," tome iii., p. 66.

CHEMICAL CHARACTERS.—This substance, like cholesterin, is a non-saponifiable fat. It has never been obtained in sufficient quantity for ultimate chemical analysis; but as in its decomposition it disengages a little ammonia, it is supposed by Verdeil and Marcet to contain nitrogen.* The evidences of this ingredient are very slight, and its existence is doubtful. It is neutral, inodorous, insoluble in water, soluble in ether, very soluble in hot alcohol but almost insoluble in cold. It is not attacked by the caustic alkalies, even after prolonged boiling. When treated with strong sulphuric acid it strikes a red color similar to that produced by sulphuric acid and cholesterin. According to Lehmann it melts at 96.8° Fahr., and on the application of strong heat may be distilled without change. Boudet extracted it from the serum of the blood by evaporating, boiling the residue with water and evaporating again, taking up the residue with boiling alcohol, which deposited the crystals on cooling.

FORM OF ITS CRYSTALS.—Boudet describes the crystals thus obtained as filaments, with varicosities here and there which gave them a beaded appearance. Lecanu also observed this peculiarity. In the atlas of Robin and Verdeil's "*Chimie anatomique*" there is a beautiful representation of the crystals of serolin from the blood. These observers have not noticed the beaded appearance mentioned by Boudet, but represent the crystals in the form of delicate transparent needles, of variable size, some very small and others quite wide, terminating in fine pointed extremities, which in some of the wider crystals is bifurcated or even trifurcated, with the edges of the larger crystals frequently split, as it were, into delicate filaments. The smaller crystals frequently arrange themselves in a fan-shape. Robin and Verdeil attribute the beaded appearance mentioned by Boudet and Lecanu to the presence of little globules of fatty matter mixed with the crystals. This seems probable, for it will be seen in examining the process of extraction employed by Boudet, that he probably did not succeed in obtaining it in a pure form. The appearance of these crystals has already been given in some of the diagrams of cholesterin, especially in Figs. 2, 6, 7,

* "*Cours de physiologie fait à la Faculté de Médecine de Paris.*" Par P. Bérard, Professeur de Physiologie, etc. Paris, 1851, tome iii., p. 118.

and 9. I have been able to follow the process of crystallization in the specimens extracted from the feces from its beginning, and have found that the splitting of the ends and edges of the crystals did not take place at first. The needles which were first formed had regular borders and single pointed extremities; but after a few days they split up in the manner described and figured by Robin and Verdeil. (See Figs. 14 and 15.)

SITUATIONS.—Up to this time, serolin (or stercorin) has been found only in the serum of the blood, and there in but very small quantity, the proportion being, according to the analyses of Becquerel and Rodier, 0.020 to 0.025 of a part per 1,000 parts of blood. They have seen it mount up to 0.060 parts, and descend to a quantity almost inappreciable.*

PROCESS OF EXTRACTION.—In the first observations I made on the blood this substance was observed before cholesterin. In these observations the blood was dried, pulverized, extracted with ether, the ether evaporated, the residue extracted with boiling alcohol and then a solution of caustic potash added which remained on the specimens for a number of days. In all the subsequent analyses of the blood cholesterin was extracted perfectly pure, and no stercorin whatever was observed. The following was the difference in the modes of analysis. In the latter case the solution of potash was not allowed to remain on the specimens more than an hour or two; but was washed away, and the residue which was left on the filter was redissolved in ether. The failure to detect the stercorin in all the later observations on the blood, which are twenty-four in number, inclines me to the opinion that it does not primarily exist in this fluid; and that when it has appeared in the extract it has been due to a transformation of a portion of the cholesterin. This view seems the more probable as I have definitely ascertained by observations on the feces, which will be detailed farther on, that cholesterin is capable of being changed into stercorin, and that this change actually takes place before it is discharged from the body. In my observations on the blood no attempt was made to get rid of this substance; and though it is

* "Traité de chimie pathologique appliquée à la médecine pratique." Par MM. Alf. Becquerel and A. Rodier. Paris, 1854, p. 62.

soluble in the menstrua which were used to extract cholesterolin and is not destroyed by any of the means that were employed to purify the cholesterolin, it never appeared in the extract. In these experiments the study of stercorin in the blood has not been attempted; and though it is not possible to state at present how the cholesterolin was transformed in the first observations, it seems most rational to suppose, in endeavoring to explain its absence in the twenty-four succeeding specimens of blood which were examined, that such a change had taken place.

I am inclined to the opinion, then, though I can not state it positively, that the substance under consideration does not exist in the blood as a proximate principle, but is formed from cholesterolin, in some unexplained way, by the processes which have been used for its extraction.* This transformation does not take place during the extraction of this substance from the feces, because I have in but a single instance been able to extract cholesterolin by the processes which are successful in obtaining it in other situations in which it exists, including meconium.

Stercorin may be extracted from the feces in the following way: The feces are evaporated to dryness, pulverized and treated with ether, which should be allowed to remain for twelve to twenty-four hours, protected from evaporation. The ether is then separated and decolorized by filtration through animal charcoal, fresh ether being added till the original quantity has passed through. It is impossible to decolorize the solution entirely, but it should be made to pass through of a very pale amber tinge and perfectly clear. The ether is then evaporated and the residue extracted with boiling alcohol. The alcohol is then evaporated and the residue treated with a solution of caustic potash, at a temperature a little below the boiling point, for one or two hours. This dissolves all the saponifiable fats, and the solution is then largely diluted with water, thrown on a filter and washed till the fluid which passes through it is perfectly clear and neutral. The filter is then dried at a moderate temperature and the residue washed

* In the absence of an ultimate analysis of this substance, it is impossible to enter into any chemical speculations in regard to the change from cholesterolin, as in the instance of creatin and creatinin or urea and carbonate of ammonia.

out with ether, which is evaporated, extracted with boiling alcohol and evaporated again. The residue is composed of pure stercorin.* The extract thus obtained is a clear, slightly amber, oily substance, of about the consistence of the ordinary Canada balsam used in microscopic preparations, and in four or five days begins to show the characteristic crystals. These are at first few in number; but soon the entire mass assumes a crystalline form. In a specimen which I extracted from the feces I have 10.417 grains, consisting, apparently, of nothing but crystals. If the extract is evaporated in a very thin watch-glass it may be examined with the microscope daily and the process of the formation of the crystals observed. These crystals, after they are fully formed, may be examined satisfactorily with a half or quarter-inch objective.

HISTORY OF SEROLIN.—Very little is to be said in regard to the history of this substance. Boudet first described it in 1833.† Lecanu confirmed these observations in 1837.‡ Since then it has been studied by Becquerel and Rodier,* Chatin and Sandras,|| W. Marcet and Verdeil.⁴ Gobley states, in an article published in the "Journal de chimie médicale," that the substance described by Boudet is not an immediate principle but a mixture of several substances, confounding it, however, with cholesterin.⁵ Robin and Verdeil adopt this view, but consider it entirely different from cholesterin.↓

This substance, existing, as it does, in large quantities in the fecal matter, must take its place among the important excrementitious matters discharged from the organism, not second in importance, even, to urea. It is a curious fact that while urea was known as an ingredient of the urine long before it could be demonstrated

* As this substance is said to be volatilized at a high temperature, it is important to avoid as much as possible the application of heat. Large quantities of it are extracted from the feces after evaporation over an ordinary water bath, but it might be better to evaporate the excrements at a lower temperature.

† Boudet. *Loc. cit.*

‡ Lecanu. "Études chim. sur le sang humain, thèse." Paris, 1837, p. 55.

* Becquerel and Rodier. "Recherches relatives à la comp. du sang." ("Comptes Rendus." Paris, 144, tome xix., p. 1084.)

|| Chatin et Sandras. "Gaz. des hôpit.," 1849, p. 289.

⁴ Bérard. *Loc. cit.*

⁵ Gobley. "Sur les matières grasses du sang." ("Journal de chimie médicale," 1851. Paris, p. 577.)

↓ Robin et Verdeil. *Loc. cit.*

in the blood, taking its name from that fluid, stercorin, an excrement of great importance, was discovered in the blood and never till now has been recognized as an excrement and an ingredient of the feces, taking a name from the serum of the blood, which does not indicate at all its excrementitious properties or the situation in which it is found in greatest abundance. As serolin has been heretofore a substance of very little prominence, and as it probably does not exist normally in the serum of the blood, and if at all, in insignificant quantity, the appellation seems a misnomer. It should be known by a name which will indicate its excrementitious properties and the channel by which it is evacuated; and I have adopted the name Stercorin * as more appropriate and more suggestive of its properties, as it is undoubtedly the most important excrement discharged by the anus.

The questions which now arise in regard to this substance open a field of inquiry too extensive, by far, to be thoroughly investigated in the time that could be devoted to this subject, or to be discussed within the limits of this paper. It would be desirable to know the full history of this product, the quantity discharged in twenty-four hours, variations that may take place with season, age, sex, diet, digestion, etc., and especially the modifications which occur in its discharge in connection with diseased conditions. These points are of great importance; but they require a long and laborious series of investigations for their elucidation. What has been done in a measure for urea must be done for stercorin, before arriving at a precise idea of its relations to disease. For this purpose a large number of quantitative analyses of healthy feces must be made and compared with similar analyses in different diseases. At present I have instituted only a sufficient number of examinations to substantiate the statements I have made in regard to the formation and discharge of this substance, and have added a few examinations of feces in disease which bear upon the same points. I hope at some future time to go more fully into the study of the feces and to contribute something toward the elucidation of some of the questions which naturally

* From Stercus, *δρις*, dung.

arise. In the mean time I present the following observations on stercorin as it appears in the feces:

EXPERIMENT IX.—Seven and a half ounces of feces, perfectly normal in appearance and being the entire quantity passed in the morning at the regular time for an evacuation, were taken from a healthy male, twenty-six years of age. After being evaporated and finely pulverized in an agate mortar, the residue weighed 2 oz. 57.313 grains. A small quantity was then extracted with alcohol, the solution being of a yellow color, and about six times its volume of ether added. The ether was filtered after standing for fifteen minutes, the filter washed with distilled water, and the solution tested with Pettenkofer's test for the biliary salts, None of these salts were present.

A watery solution was then made of another portion, which was filtered and tested with nitric acid, but failed to show the reactions of the coloring matter of the bile.

The dry residue was then treated with five fluidounces of ether for twenty hours, when it was filtered through animal charcoal, fresh ether being added till the fluid which passed through made five ounces. It came through perfectly clear and of a very light golden tinge. It was then evaporated, leaving a golden yellow fat with a number of whitish resinous masses. It was then extracted with 3jss of boiling alcohol, which removed everything but a small quantity of bright yellow oil, and filtered while hot. It became turbid on cooling and was set aside to evaporate. Both the ethereal and alcoholic extracts had a very offensive rancid odor. The residue, after the evaporation of the alcohol, consisted of a considerable quantity of fat of a yellowish color and of a consistence like thick turpentine. It was then treated with a solution of caustic potash, kept near 212° for about thirty minutes and allowed to stand for twenty hours. At the end of that time a large quantity of fat floated on the top of the fluid not at all affected by the alkali. It was then largely diluted with distilled water filtered and washed, the filter dried, and the residue redissolved in ether. This ethereal solution was evaporated and the residue extracted with boiling alcohol as before. After the alcohol had evaporated, a small quantity was treated with sulphuric acid which produced a peculiar red color similar to that produced when the acid was added to a specimen of cholesterin, extracted from the blood and used for purposes of comparison.

Five days after, the specimen was examined with a $\frac{1}{8}$ th inch objective and presented some crystals which looked like serolin; but it was impossible, on account of the thickness of the glass capsule, to apply a sufficiently high power to make this certain. Some long, pale, radiating crystals were observed, composition unknown, but they were not the crystals of excretin described by Marcet.*

* Marcet, in two papers published in the "Philosophical Transactions" for 1854 and 1857, describes a new proximate principle in the feces which he calls Excretin. This he obtains in the following way: He first treats the feces

The specimen was treated again with a solution of caustic potash and kept at nearly the boiling point of water for three and a quarter hours, most of the fat floating on the top of the fluid in white flakes and yellow drops, but a considerable quantity undergoing saponification, as evidenced by the color of the potash solution. The potash was then removed by filtration, the residue dissolved in ether and extracted with boiling alcohol as before.

Four days after the evaporation of the alcohol, a large number of the characteristic crystals were formed. These did not have the split extremities and edges noted by Robin, but terminated in a single point and had regular borders. The crystals are represented in Fig. 14.

In a few days the entire mass had assumed a crystalline form, and the crystals then presented split extremities and borders such as are mentioned by Robin. (See Fig. 15.)

The quantity of stercorin was 10.417 grains.

EXPERIMENT X.—Another analysis was made of the feces from the same individual. During the experiment a large quantity was unfortunately lost, and the examination, therefore, was not quantitative. The presence of stercorin was established.

EXPERIMENT XI.—The feces of the dog from which blood of the carotid and internal jugular on one side had been taken fifteen days before, the animal having entirely recovered, were examined. The analysis was not quantitative. The feces were treated in the way already described and the presence of stercorin determined.

EXPERIMENT XII.—A specimen of feces voided by a healthy dog, fasting, was examined in the usual way for stercorin. After the final extract had evaporated, it was examined microscopically and found to contain, in addition to stercorin, a considerable quantity of cholesterin, crystallized in beautiful tablets. This is the

with boiling alcohol till nothing more can be extracted. A sediment deposits from the alcohol on cooling. The alcoholic solution is acid. Milk of lime is added to the solution, which gives a yellowish-brown precipitate, leaving a clear straw-colored fluid. The precipitate is then collected on a filter, dried, afterwards agitated with ether and filtered, forming a clear yellow solution. In one to three days, beautiful silky crystals collect in masses, or tufts, adhering to the sides of the vessel, throwing out ramifications in every direction. These, viewed under the microscope, are in the form of acicular, four-sided prisms, and this substance is called by Dr. Marcet, excretin, and is found nowhere but in the feces. It is soluble in ether and hot alcohol, sparingly so in cold alcohol, and insoluble in hot or cold water. It does not crystallize from an alcoholic solution on cooling but crystallizes from ether. When suspended in boiling water it fuses into resinous masses, and floats on the top. Its fusing point is 203° to 205° Fahr. It may be boiled for hours with potash without undergoing saponification.

In the article published in 1857, Dr. Marcet gives the composition of the excretin $C_{78}H_{78}O_2S_1$.

There is no similarity between the form of the substance described by Marcet and stercorin. Its high fusing point, 203° to 205° Fahr., and its crystallization from an ethereal solution, also serve to distinguish it from stercorin, which fuses at 96.8° Fahr. and does not crystallize from an ethereal solution.

only examination of feces in which I have found cholesterin. The proportion of stercorin and cholesterin was as follows:

Quantity of feces.....	137.513 grains.
Stercorin with a little cholesterin.....	0.216 "

These examinations of the feces in health show that they invariably contain a non-saponifiable substance known under the name of serolin, but which I have called stercorin. In but one of these analyses, the last, did I find any cholesterin, though the first were originally undertaken with a view to the extraction of this substance.

Stercorin has never before been detected in the feces; and, so far as my knowledge of its physiological properties is concerned, it may be considered a new substance, the discovery of which, in this situation, marks it as one of the most important of the products of destructive assimilation. The next question which arises, then, is in regard to its origin.

ORIGIN OF STERCORIN.—In the study of the chemical properties of this substance, it has been seen that it is one of the non-saponifiable fats, having many characters in common with cholesterin. It has been described, under the name of serolin, as found in the blood in minute quantity, but it does not exist in any of the fluids which are poured into the alimentary canal. Cholesterin, however, which it so closely resembles, is one of the constituents of the bile. The fact that cholesterin is discharged into the small intestine and is not usually found in the evacuations, while stercorin is abundant, would at once point to a possible connection between these two substances. In most cases, in health, cholesterin disappears and stercorin is found; but in some rare instances, as in the single examination of dogs' feces (Experiment XII.), the two substances coëxist in the evacuations, stercorin, in the example just mentioned, in much the greater quantity. The question then arises: Is cholesterin capable of being converted into stercorin, and does the latter substance originate from a transformation of the cholesterin of the bile? Before treating of this subject experimentally, I shall examine the facts already ascertained bearing on this point. No examinations of the feces have ever been made for stercorin; but under certain conditions cholesterin has been found discharged by the anus without alteration.

Cholesterin has already been found in the meconium, in the feces of hibernating animals and occasionally in ordinary feces.

MECONIUM.—Cholesterin exists in meconium in considerable quantity, where it may be seen in tablets in a simple microscopic examination, and from which it may be extracted in quantity and with great facility. Stercorin (or serolin) has never been mentioned as existing in this situation. In the single examination I have made of the meconium, I found an abundance of cholesterin, 6.245 parts per 1,000, but no stercorin. There is no difficulty in explaining the origin of the cholesterin in meconium. Long before any food is taken into the alimentary canal and before the exclusively digestive fluids are formed, the bile is secreted and discharged. It accumulates in the intestine, with other matters constituting the meconium, and is finally evacuated soon after birth. Hence cholesterin exists in large abundance; but when the digestive fluids are secreted and food is received into the alimentary canal, the cholesterin is lost and stercorin makes its appearance.

FECES OF HIBERNATING ANIMALS.—As the excretory function of the liver begins before food is taken into the alimentary canal, so it goes on during the state of hibernation, when the animal takes no food for weeks or even months. Under these conditions, cholesterin is found unchanged in the feces; but it disappears when the animal arouses and the digestive organs resume their functions.

NORMAL FECES.—In the normal feces cholesterin is generally absent; but in Experiment XII., it was found in small quantity, mixed with stercorin. This animal had been certainly twenty-four hours, and probably forty-eight hours without food. The feces were of normal color and consistence.

These facts seem to show that before digestion begins, as in the foetus, and when it is suspended, as in hibernating animals and in Experiment XII., cholesterin passes through the alimentary canal unchanged; but so soon as digestion begins, cholesterin is lost in the feces and its place is supplied by stercorin. It seems almost certain, then, that in its passage down the alimentary canal, the cholesterin of the bile is acted upon by some of the digestive fluids and changed into stercorin. This change

seems to be incident to the digestive act; for before digestion begins and when it is suspended, cholesterin passes through unchanged. A conclusive observation would be to cut off the bile from the intestines, and consequently the cholesterin, and note the effect upon the production of stercorin. In a case of jaundice from duodenitis (which will be more minutely detailed in the section on the pathological relations of cholesterin), the necessary conditions for this observation seemed to be fulfilled. The patient suffered from intense jaundice dependent upon obstruction of the common bile duct from duodenitis. The feces were clay-colored. After a time the patient was relieved of the jaundice, and the feces regained their natural color. While the feces were decolorized and when the icterus was most marked, it is probable that the bile was entirely cut off from the alimentary canal. This condition was relieved, however, when the feces regained their color and the icterus disappeared. For the purpose of ascertaining the effect of the obstruction to the flow of bile on the stercorin of the feces and of the reestablishment of the flow, the stools were examined chemically during the jaundice and after the patient had recovered.

ANALYSIS OF DECOLORIZED FECES.—The quantity of feces examined was 941.4 grains. After evaporation, extraction with ether and extraction of the residue left after the evaporation of the ether with hot alcohol, the fat, which was very abundant, was entirely saponified by boiling for fifteen minutes with a solution of caustic potash, showing that neither cholesterin nor stercorin was present.

ANALYSIS OF FECES FROM THE SAME PATIENT AFTER THEY HAD BECOME NORMAL IN COLOR.—This was made nineteen days after the preceding analysis. The quantity of feces was small. The specimen was treated in the usual way, showing stercorin in the following proportion:

Quantity of feces.....	502.00 grains.
“ “ stercorin.....	0.34 “

Taken in connection with the facts which have already been cited in regard to the discharge of cholesterin by the anus when digestion is not going on, this observation seems to establish the origin of stercorin. It is produced by a transformation, connected with the digestive act, of

the cholesterin of the bile. When cholesterin does not find its way into the alimentary canal, as was the case in the first analysis of feces, stercorin is not found in the dejections; when the discharge is reëstablished, the stercorin reappears.

COMPARISON OF THE DAILY QUANTITY OF STERCORIN DISCHARGED, WITH THE QUANTITY OF CHOLESTERIN PRODUCED BY THE LIVER.—The quantity of stercorin which I extracted from the regular daily feces of a healthy adult male was 10.417 grains. As there is no cholesterin found in the dejections, this should represent the entire quantity of cholesterin excreted in the twenty-four hours. A comparison of this quantity with the estimated quantity of cholesterin discharged in the day, shows this to be the case.

Quantity of bile in the twenty-four hours (Dalton).....	16.940 grains.*
“ “ cholesterin at 0.618 pts. per 1,000 (Flint).....	10.469† “
“ “ stercorin discharged (Id.).....	10.417 “
Difference.....	.052

This insignificant difference of 0.052 of a grain shows at once the correctness of the estimate of the daily quantity of bile excreted, the accuracy of the estimate of the proportion of cholesterin in the bile and of the quantitative analysis for stercorin; and made, as the three observations were, without the slightest reference to each other, adds the final link to the chain of evidence in support of the view that cholesterin, in its passage down the alimentary canal, is converted into stercorin, in which form it is discharged in the feces.

The history of cholesterin thus resolves itself:

1. Cholesterin is an effete material, produced by the destructive assimilation of nervous matters and absorbed by the blood.
2. It is separated from the blood in its passage through the liver and enters into the composition of the bile, giving this fluid its excrementitious character.
3. It passes with the bile into the upper part of the small intestine, when the process of digestion induces a change into stercorin, in which form it is discharged by the feces.

* Dalton, "Treatise on Human Physiology," 2d edition, p. 171.

† See table, p. 173.

4. Stercorin, the principal excrementitious constituent of the feces, is one of the most important excretions produced by the waste of the system.

PATHOLOGICAL RELATIONS OF CHOLESTERIN.—With the limited data on the subject of the variations in the quantity of cholesterol in health and disease, it is impossible to do more than merely to open the subject of its pathological relations. To a certain extent, all questions in physiology have for an end the elucidation of points in pathology. The practical physician who may be the reader of this article will naturally inquire if the more definite views which we are now enabled to hold in regard to the function of the bile are of any use to him in the study and treatment of disease. It is certain that no addition to a knowledge of the functions of the healthy body is without its bearings on disease, immediate or remote. What may seem to be simply a matter of interest to the pure physiologist, without apparently any practical bearing, is sure at some time to become so connected with other advances as to be useful to the practitioner. But the pathological relations of an important excretion do not have a practical interest so remote, especially when this function is connected with the liver. Almost from time immemorial, a large number of diseases have been referred to derangement of the liver, and in their treatment, it has been thought of immense importance to promote the secretion of the bile. A certain class of remedies supposed to regulate the secretion of bile has been constantly employed by physicians. At the present day these ideas have fallen somewhat into disrepute; for the enlightened physician is now accustomed to base his pathological views upon a certain amount of definite knowledge; and it has been found that both the physiology and the pathology of the bile have been very little understood. The older practitioners had, as we have now, a certain class of cases characterized by a general malaise, and having indefinite symptoms that were attributed to "biliousness," in which they were in the habit of employing the cholagogues, with mercury at the head, with undoubted success. It is true that as knowledge of disease becomes more accurate, the conditions which were supposed to indicate "biliousness,"

have been referred to other disorders; but no great advance has been made in the pathology of the liver, and there are yet many conditions which may be successfully, though empirically, treated, the true character of which is unknown. It is on this obscure subject that it is hoped the preceding physiological investigations will throw some light. To repeat a comparison made use of before, a knowledge of the functions of cholesterin and its history in the healthy organism should contribute as much to the pathology of diseases dependent on derangement of this function as the development of the functions of urea has for diseases now known to be dependent on uremia.

CHOLESTEREMIA

In common with other excrementitious substances, which invariably exist in the blood in health, if the function of the eliminating organ is interfered with, accumulation takes place in the blood. This has already been incidentally referred to in treating of the properties of cholesterin which allied it to effete substances. It takes place as regards urea; but cases of uremic poisoning occurred and patients died in uremic coma, long before the cause of it was understood. It is the same with the bile. Ordinary cases of jaundice, which have been called by Piorry cholemia, are not of a dangerous character; but there are cases in which jaundice, though less marked as regards color, is a very different condition. Here is evidently the operation of some poison in the blood; and coma and death from its effects on the brain follow as in retention of the urea. Pathologists inquire why there is this difference in the severity of cases of icterus. Chemists have analyzed the blood in the hope of explaining it by the presence of the glycocholates and taurocholates of soda in the grave cases, regarding them as the only important constituents of the bile; but their failure to detect these substances has left the question still unanswered.

In cases of simple jaundice there is a resorption of the coloring matter of the bile from the excretory passages.

In cases of grave jaundice, which almost invariably terminate fatally, there is retention of cholesterin in the blood, or cholesteremia.

I have been forced to make use of cases of disease exclusively in studying this condition, for no one has yet been able, in the larger animals, to extirpate the liver, notice the symptoms of poisoning and demonstrate the accumulation of cholesterin in the blood. Nor have I yet been able, on account of the insolubility of cholesterin, to make experiments by injecting it into the circulation. I had, however, an opportunity of making an examination of the blood of a patient in the last stages of cirrhosis of the liver accompanied with jaundice and compare it with an examination of the blood of a patient suffering from simple icterus. Both of these patients had decoloration of the feces; but in the first, the icterus was a grave symptom, accompanying the last stages of disorganization of the liver; while in the latter, it was simply dependent on duodenitis, the prognosis was favorable and was verified by the result. As icterus accompanying cirrhosis is of infrequent occurrence, I deemed myself fortunate in having an opportunity to compare the two cases.

CASE I. JAUNDICE DEPENDENT ON OBSTRUCTION FROM DUODENITIS.—Mary Bishop, æt. 42, native of Ireland, widow, occupation servant, was admitted into the Blackwell's Island Hospital, June 12, 1862, with the following symptoms: Slight febrile movement, with severe pains over the duodenum; the surface of the body was highly icteric; the stools were clay-colored; urine high-colored, but not examined for bile; lungs and heart normal; appetite rather poor; no ascites. The icterus had existed since about May 23, 1862. The patient was confined to the bed.

Dr. Flint, the visiting physician, pronounced it a case of icterus dependent on duodenitis.

TREATMENT.—Laxatives daily, with good diet and a moderate quantity of stimulus.

June 21. A small quantity of blood was drawn from the arm for examination, and on June 23, the feces were collected for the same purpose.

June 27. The patient remains about the same.

July 11. All pain and tenderness over the duodenum have disappeared. She has steadily improved since the last record. The stools have been natural for several days. Though confined to the bed most of the time, she is able to sit up two or three hours daily. The jaundice has been gradually diminishing, and three or four days ago it had entirely disappeared and is now absent.

July 12. Another specimen of the feces, which was of normal appearance, was taken for examination.

ANALYSIS OF THE BLOOD FOR CHOLESTERIN.—The blood was examined about sixteen hours after it was taken from the arm. It had

fully separated into serum and clot. The serum was of a bright yellow color, more markedly bilious than in the succeeding case. It was evaporated, pulverized, and a quantitative analysis for cholesterol made, with the following results:

Quantity of blood.....	212.428 grains.
Quantity of cholesterol.....	0.108 "
Proportion of cholesterol per 1,000 pts. of blood	0.508 "

CASE II. JAUNDICE WITH CIRRHOSIS.—Ann Thompson, æt. 39, native of Ireland, occupation servant, was admitted into the Blackwell's Island Hospital June 16, 1862, and gave the following history:

Three months ago she contracted a severe cold, which was accompanied with swelling of the left hand and of both legs, continuing for eight or nine weeks. At the end of that time she noticed that the abdomen was increasing in size. She was then very weak, the urine was scanty, bowels regular up to the time when she entered the hospital. She denied having been in the habit of drinking spirit, but acknowledged that she drank beer.

June 18. The surface of the body was icteric, the color was very marked under the tongue and in the conjunctiva; the abdomen was full of fluid; pulse 90, small and weak; bowels loose and the dejections clay-colored; the urine highly tinged with bile and copious; appetite very poor. She was tapped, and about eight quarts of clear, straw-colored serum were evacuated. The patient was confined to the bed.

Dr. Flint, the visiting physician, diagnosticated cirrhosis.

The treatment consisted of sustaining measures, with stimulants and the tinct. ferri muriat.

June 21. A small quantity of blood was taken from the arm for examination, and on June 23, a specimen of the feces was obtained for the same purpose.

The patient died June 27. There were no convulsions, and she was sensible, though in a state of stupor, up to twenty minutes before the fatal termination. The stupor existed three or four days before death. Two days before, she complained of double vision. The icterus was excessive up to the time of her death.

AUTOPSY.—The abdomen contained about twelve quarts of liquid. The liver was examined. Its weight was 3 lbs. 12½ oz. It was very light-colored, and had something of the "hob-nail" appearance, presenting, in short, the gross characters of cirrhosis. The gall-bladder was very much contracted and contained only about two drachms of bile. Microscopic examination of the organ showed the liver-cells shrunken. The fibrous substance was increased in quantity, and there were present a large number of rather angular globules of fat.

ANALYSIS OF THE BLOOD FOR CHOLESTERIN.—The blood was examined about sixteen hours after it was drawn. It had fully separated into serum and clot, and the serum was of a greenish-yellow color. The whole, serum and clot, was then evaporated, pulver-

ized, and a quantitative analysis made for cholesterin in the manner already indicated, with the following results:

Quantity of blood.....	50.776 grains.
Quantity of cholesterin.....	0.093 "
Proportion of cholesterin per 1,000 pts.....	1.850 "

The following table gives a comparison of these results with those obtained in the analyses of the three specimens of healthy blood from the arm, which were examined at the same time, and all five specimens subjected to identical processes.

TABLE OF QUANTITY OF CHOLESTERIN IN HEALTHY BLOOD, BLOOD FROM SIMPLE JAUNDICE, AND JAUNDICE WITH CIRRHOSIS

HEALTHY BLOOD		BLOOD OF JAUNDICE	
	Cholesterin per 1,000 pts.		Cholesterin per 1,000 pts.
Male, æt. 35.....	0.445	CASE I. Simple jaundice	0.508
" " 22.....	0.658	" II. Jaundice with	
" " 24.....	0.751	cirrhosis....	1.850

CASE I. Simple jaundice.	Percentage of increase over minimum of healthy blood.	14.157
	Decrease below maximum...	32.357
CASE II. Jaundice with cirrhosis.	Increase over minimum	315.730
	Increase over maximum	146.338

The results of the examination of the blood in these cases of disease are striking and instructive. It has already been seen that the variations in health are very considerable. In the three analyses here noted, the maximum was 0.751, and the minimum 0.445 pts. per 1,000. The conditions which regulate this variation it has not yet been possible to study; but enough is known in regard to it, to see that in the examination of blood in disease, the cholesterin must mount considerably above the maximum or fall much below the minimum, to be considered beyond the limits of health. But in the second specimen of jaundiced blood, the variation from the limits of health is so considerable as to admit of important physiological and pathological deductions.

In the first place, what is the bearing of these observations on the physiology of cholesterin? As before remarked, no one has been able to remove the liver from a living animal and note the effect upon the quantity of cho-

lesterin in the blood.* This experiment, if it were possible, and if it showed that cholesterin increased in quantity and killed the animal, would go to show that it was an excrementitious substance and that it was removed by the liver. But while the experimental physiologist contributes much to the information of the pathologist by artificially producing abnormal conditions, pathology furnishes a multitude of useful experiments of Nature, which are invaluable to the physiologist. In the present instance, cases of disease of the liver present a condition which can not at present be imitated by experiments on the lower animals. Disorganizing disease of the liver must interfere with its excretory function, as Bright's disease does with the elimination of urea; and if cholesterin is an excrementitious substance to be removed by the liver, when the liver is seriously affected with structural disease there should be an accumulation of it in the blood. This, if fully established, is positive proof of the character of cholesterin and the function of the liver connected with its elimination.

What is to be learned, then, from a comparison of the blood in Case II. of jaundice dependent on cirrhosis with healthy blood and a study of the history of the case?

The cholesterin, in this instance, is enormously increased in quantity, 315.730 per cent. over the minimum, and 146.338 per cent. over the maximum. The case, as far as symptoms are concerned, was of a very grave character. The patient not only suffered from an accumulation of liquid, but there was evidently a poison in the system. The patient died after three or four days of stupor, and on post-mortem examination the liver was found disorganized. There was a deficient secretion of bile, and had been for a long time; for the gall-bladder was much contracted and the stools were clay-colored. In short the patient died of cholesteremia; and the fact that this condition can exist is a proof of the excrementitious function of

* Müller, Kunde and Moleschott have succeeded in removing the liver from frogs and keeping them alive for two or three days—Moleschott preserving them for several weeks. These observations were made with reference to the accumulation of the biliary salts and of the bile pigment in the blood, their attention not having been directed to cholesterin. I began a series of experiments on frogs, but they promised to be so prolonged that they were deferred.

cholesterin, as uremia, as a toxemic condition, shows that urea is an excretion.

Physiologically considered, this case fulfils an essential condition of excrementitious substances; namely, accumulation in the blood when the eliminating functions of the excretory organs are interfered with. The liver became so disorganized that its functions were seriously disturbed, and the quantity of cholesterin in the blood increased to a very great extent.

The pathological deductions from the facts which have been elicited by examinations of the blood in these cases seem to me of great importance. The literature of diseases connected with disorders of the liver is full of theories, more or less plausible, to explain certain conditions which have long been established by clinical observation. There are cases of simple jaundice which are not dangerous to life, and sometimes, though the icterus is excessive, run a certain course without interfering even with the ordinary vocations of the patients. Again, there is jaundice which is invariably fatal. The disease described by Frerichs under the name of acute atrophy of the liver, and called by some, acute jaundice, is one of the most serious diseases of which there is any knowledge. The existence of this great difference has led clinical observers to attribute the mild cases to simple resorption of the coloring matter of the bile, and the severe cases to a retention or resorption of some of its more important constituents; especially as it has also been observed that the symptoms which characterize the latter condition occasionally occur in structural diseases of the liver without any discoloration of the skin. But the pathology of this disease has been entirely unknown. It has been thought that in such cases some of the elements of the bile should exist in the blood. Frerichs says: "In the same way that urea accumulates in large quantity in the blood in granular degeneration of the kidneys, so ought the biliary acids and bile-pigment to accumulate in the blood in cases of granular liver. Repeated observations have proved that this is not the case." * Experiments on animals have been followed with like re-

* "A Clinical Treatise on Diseases of the Liver," by Dr. Fried. Theod. Frerichs, Professor of Clinical Medicine, etc., Berlin. Translated by Charles Murchison, M. D. "The New Sydenham Society," London, 1860, vol. i., p. 83.

sults. The frogs that were kept alive by Moleschott for weeks after the removal of the liver did not present a trace of the biliary salts or bile-pigment in any part of the system, showing that these matters are manufactured in the liver. This obscurity, which leads to all sorts of theories in regard to liver-pathology, must exist so long as our knowledge of the physiology of the bile is so indefinite. If observers had looked for cholesterin, a substance which preëxists in the blood and is separated by the liver, instead of the biliary salts, which do not pre-exist in the blood, are manufactured in the liver, as these experiments tended to show, and are peculiar to the bile, they would have met with different results. The very fact that the biliary salts are peculiar to the bile and found in no other fluid should have led them to disregard these substances in their analyses of the blood, because this stamps them as secretions and distinguishes them from excretions. They should have looked for some substance which exists in the blood as well as the bile, an indispensable condition of an excretion, and this substance is cholesterin.

Understanding, therefore, the physiological relations of cholesterin, jaundice may be divided into two varieties: simple icterus, or yellowness, and a condition which I have called cholesteremia. Cholesteremia may occur, also, without discoloration of the skin.

SIMPLE ICTERUS.—In simple icterus there is a resorption of the coloring matter from the biliary passages. As it has been shown that the coloring matter of the bile appears first in the liver, when it exists in the blood it is not due to accumulation but to resorption. In these cases the resorption is generally due to obstruction of the biliary passages. The patient suffers only from the disease which causes the obstruction, and from the derangement of digestion which is due to the absence of bile from the intestinal canal. In those cases in which there is no organic disease of the liver, there is no danger of absorption of cholesterin. This is a condition analogous to retention of urine. The patient suffers simply from retention of bile in the excretory passages, and cholesteremia is no more to be expected from obstruction of the bile-duct without structural changes of the liver, than uremia is to be looked for in vesical retention of urine without organic

change in the kidneys. Excretions are not reabsorbed, although they may be retained in the blood.

The quantity of cholesterin in the blood is not necessarily increased in simple icterus; for the liver is still performing its function of elimination, and when once separated from the blood it is not taken up again. The analysis of the blood in Case I. indicated a proportion of 0.508 parts per 1,000, which is within the limits of health, a little below the mean, probably on account of the somewhat enfeebled condition of the patient.

The feces may or may not be decolorized, this depending on the extent of the obstruction to the passage of bile into the intestine. The obstruction to the flow of bile frequently is relieved before the system has time to remove the coloration of the skin, and the feces become normal while the patient is icteric. In some instances there is no change in the appearance of the dejections during the course of the disease. When the dejections are entirely decolorized there is an absence of stercorin, into which the cholesterin is transformed before it is discharged, with an abnormal quantity of fat which has passed through undigested.* Stercorin reappears in the feces when the flow of bile is reëstablished and they assume their normal color.

The two following analyses were made of the feces in Case I.: one, when they were entirely decolorized and the patient was very much jaundiced, and the other, when she had recovered and the dejections had assumed their natural appearance.

FECES OF CASE I. JAUNDICE DEPENDENT ON DUODENITIS. FIRST ANALYSIS.—The feces were clay-colored and apparently free from bile. They weighed 941.4 grains. They were evaporated to dryness without difficulty, pulverized, digested with fʒij of ether for twenty hours, filtered through animal charcoal, evaporated and extracted with hot alcohol. The fatty residue after evaporation of the alcohol was very abundant.

The residue was then treated with a solution of caustic potash and exposed to a gentle heat. In fifteen minutes it became entirely saponified, forming a clear homogeneous soap with no residue, showing the absence of stercorin. The soap was boiled down and

* This fact, which has often been remarked, seems to indicate that the bile is actively concerned in the digestion of the fats. I have noticed that dogs with biliary fistulæ, though with a ravenous appetite, refuse to eat fat meat. This disinclination to eat fat has been noticed in cases of jaundice with decoloration of the feces.

molded into a cake, which I preserved and which weighs thirty-four grains. The following is the result of the examination:

Quantity of feces.....	941.4 grains.
" " fat.....	39.124 "
Percentage of fat.....	4.144
No stercorin or other non-saponifiable fats.	

FECES NINETEEN DAYS AFTER. SECOND ANALYSIS.—At that time the patient had entirely recovered from the jaundice, and the feces had regained their natural appearance. A small specimen was taken for chemical examination, which was made, employing the process already described for the extraction of stercorin, with the following result:

Quantity of feces.....	503 grains.
" " stercorin.....	0.340 "

CHOLESTEREMIA WITH ICTERUS.—In jaundice complicated with blood-poisoning there exists a very different state of things as regards gravity of symptoms and prognosis. This occurs in acute jaundice, or when it accompanies and is dependent upon structural change in the liver, as the jaundice of cirrhosis. The difference in the pathology of these cases, compared with those of simple icterus, has long been recognized; but, as before remarked, analysis of the blood has failed to throw any light on the subject, because chemists directed their attention exclusively to the biliary salts. Frerichs says:

"I have myself repeatedly examined jaundiced blood, which has been obtained by venesection, or still more frequently, from the heart or vena cavæ of the dead body, for the biliary acids, and their immediate derivatives; and more recently I have had it examined by my assistant, Dr. Valentin, but always with negative results. No substance could be found in the alcoholic extract of the blood which yielded any indication, by Pettenkofer's test for the biliary acids, whether this alcoholic extract was treated directly with sulphuric acid and sugar, or whether, in order to get rid of foreign substances, a watery extract of it was first prepared. This coincides with the experience of most of the older observers."*

In cases of blood-poisoning by retention and accumulation of elements of the bile in the blood, the important pathological condition is a great increase in the quantity of cholesterin. The fact of accumulation of this substance in the blood in certain cases of icterus, has been noticed by Becquerel and Rodier; but they did not connect it with structural change in the liver and did not explain its physi-

* Frerichs, *op. cit.*, p. 95.

ological or pathological importance. The fact of its accumulation in the blood is strong evidence of its excrementitious character; but this does not appear to have attracted the attention of the observers just mentioned. The following is one of the cases in which increase of cholesterin was observed by them, the only one in which they allude to its significance, and here merely to state their inability to explain it:

"The second case is nearly similar, excepting the phlegmasia, which did not exist. It relates to a boy, nineteen years of age, a *limonadier*, affected for some time with a bilious diarrhoea, with fever, and icterus, recently developed and very marked. There existed in the blood of this patient a slight diminution of the globules (136); albumen in normal quantity (71.4); likewise fibrin (2.3); fatty matter sufficiently abundant; serolin in an imponderable quantity; cholesterin excessively abundant (0.798); soaps abundant (2.032). To what cause must we attribute this great quantity of cholesterin? How and why is it concentrated in the blood in spite of the biliary flux? This is what it is difficult to decide."*

What I have shown in regard to the physiology of cholesterin removes the difficulty in the explanation of this fact. In Case II. there was the rare complication of jaundice with cirrhosis, the symptoms evidently pointing to poisoning by retention of some toxic element in the blood. Examination of the blood in this case showed that cholesterin existed in the proportion of 1.850 parts per 1,000; the minimum of healthy blood being 0.445 and the maximum 0.751 parts. Taking this case as an example, there is cholesteremia with jaundice, presenting symptoms which characterize the retention of bile in the blood, which are already well known and were established long before it was possible to say what toxic element was retained. Cases in which jaundice exists with cholesteremia are so different from cases of ordinary jaundice that there is no difficulty in making the discrimination by symptoms. When jaundice exists with cirrhosis, it is probable that there always is cholesteremia. In acute jaundice the symptoms, especially those referable to the nervous system, are so marked that the gravity of the case is easily recognized. I have no doubt that in such cases cholesterin is immensely increased in the blood, although on account of their rarity I have not had an opportunity of determining this by analysis.

* Translated from Becquerel and Rodier, *op. cit.*, p. 210.

Icterus with cholesteremia and simple icterus are quite distinct from each other. The only feature they have in common is the discoloration of the skin. Simple icterus, which is comparatively harmless, is not likely to run into the more severe variety, which can not occur without structural change in the liver; while the grave variety occurs when there is evidence of organic disease of the liver or when the case presents symptoms from the first which indicate its serious character. The one has no more constitutional danger than exists in a simple case of spasmodic retention of urine; while the other has characters as grave as those which attend uremic poisoning due to disorganization of the kidney.

In these cases the feces may show a very marked deficiency of bile; but this is due to the deficient, but not arrested secretion of this fluid, while the clay-colored stools in simple icterus are dependent on the want of discharge of the bile into the intestine. While in the latter instance, as in Case I., one would expect to find no stercorin in the dejections, in the former, one would expect to find stercorin, though in greatly diminished quantity. Further examination of the feces in cases of structural disease of the liver will be of advantage as indicating, by the quantity of stercorin found, the extent to which the eliminative function of the liver is disturbed.

The following analysis was made of the feces in Case II. of jaundice dependent on cirrhosis:

FECES OF CASE II. JAUNDICE DEPENDENT ON CIRRHOSIS.—The feces were clay-colored, though the decoloration was not quite so marked as in the Case I. of simple jaundice.

The specimen was evaporated with great difficulty. It was reduced to a black, glutinous mass which could not be pulverized. It was treated twice with alcohol, the alcohol evaporated, and once with ether. After the ether had evaporated the residue was pulverized and analyzed for stercorin, with the following result:

Quantity of feces.....	272.1	grains.
Stercorin.....	0.077	"

This analysis showed a very great diminution in stercorin in the feces, the normal quantity in the daily passages, according to the single examination I have made, being 10.417 grains. The specimen of feces was the ordinary quantity passed daily. It showed that cholesterin

was still eliminated, though not with sufficient activity to prevent its accumulation in the system. This was further evidenced by the post-mortem examination, when the gall-bladder was found contracted but containing a small quantity of bile.

Examination of the blood and feces of the patient suffering from cholesteremia with jaundice thus leads to the following conclusions:

1. Cholesterin was largely increased in the blood showing that the structural change in the liver had interfered with its elimination.

2. Stercorin was correspondingly diminished in the feces, showing that the cholesterin was not discharged in normal quantity into the alimentary canal.

CHOLESTEREMIA WITHOUT ICTERUS.—From a practical point of view, this condition is one which it is very important to be able to recognize; but here is felt most the necessity of more extended investigations than it has been possible to make. I have been able only to open the subject by the analysis of one or two specimens of blood taken from patients who had organic change in the liver, but no jaundice. One of the most familiar of these affections of the liver consists in those changes of structure included in the term cirrhosis. Frerichs describes a condition which he calls acholia, denoting suppression of the functions of the liver. This is the condition which I have called cholesteremia, which expresses the constituent of the bile which produces the toxic effects, the action of which was unknown to Frerichs; while the term acholia expresses retention of bile without giving any idea of the active morbid agent. Further investigation will undoubtedly establish more fully what the analyses I have made thus far seem to show; namely, that in what Frerichs calls acholia without jaundice, there is the cholesteremic condition that exists in acholia with jaundice. The following quotation from Frerichs' treatise on the liver gives an idea of one of the conditions in which there is acholia (or cholesteremia) with or without jaundice.*

"Cases have repeatedly occurred to me, in which individuals who for a long period have suffered from cirrhosis of the liver,

* Frerichs, *op. cit.*, p. 241.

have suddenly presented a series of symptoms which are foreign to that disease. They have become unconscious, and have been afterwards seized with noisy delirium, from which they passed to deep coma, and in this state have died. In one case there was spasmodic contraction of the muscles of the left side of the face. In most cases, slight jaundice made its appearance at the same time, and in one instance there were petechiæ. Upon post-mortem examination, not the slightest lesion could be detected in the brain, neither were there indications of any acute disease which could account for the derangement of the cerebral functions. The liver, in all cases, presented cirrhotic degeneration in a marked degree, and the glandular cells were for the most part loaded with fat; large quantities of leucine separating from it; the bile ducts contained only a small quantity of pale bile."

In certain cases of organic disease of the liver, and probably in all cases accompanied by the grave symptoms mentioned by Frerichs, there is cholesteremia; but this character does not exist in all cases where the liver is affected, any more than uremia exists in all cases of structural disease of the kidney. Nature not only provides organs which are sufficient for the removal of effete matters from the blood, but provides for conditions in which the function of these organs may be partly interrupted, and yet the excretion go on, a part taking on the function of the whole. One of the kidneys may be removed, and yet the other, increased in size it is true, is capable of performing the function of both. The kidneys may be partially disorganized, and yet the sound portion be sufficient for the depurative function, and urea will not accumulate in the blood. So it is with the liver. There are patients with partial disintegration of this organ, as in some cases of cirrhosis, suffering apparently but little inconvenience from the disease and presenting none of the symptoms of cholesteremia. But when the liver is extensively affected, so much so that it can not separate the cholesterin effectually from the blood, there is cholesteremia. I have made an analysis of the blood of two patients affected with cirrhosis who presented this contrast as regards the symptoms of cholesteremia. In one of them, Case III., there was considerable constitutional disturbance; and in the other, Case IV., the patient was about and suffered no great inconvenience, though he had been tapped for ascites more than thirty times.

CASE III. CIRRHOSIS WITH ASCITES AND CONSIDERABLE AFFECTION OF THE GENERAL HEALTH.—Mary Perkins, æt. 23, native of Ireland, prostitute, has been a spirit-drinker for about seven years. About the 1st of May, 1862, she noticed an enlargement of the abdomen, which was accompanied with pain over the region of the liver, when she took to the bed. She states that at that time the stools were dark green. Fluid continued to accumulate in the abdomen, and was drawn off in the hospital (Blackwell's Island), June 25. About six quarts of a clear, straw-colored serum were removed, but a little was left in the abdomen, as the patient was very weak. The patient improved after the removal of the fluid, which did not reaccumulate in any considerable quantity. The liver was found diminished in size, and from this and other circumstances, the diagnosis was cirrhosis.

June 28. A specimen of blood was taken from the arm for examination. She left the hospital July 6, and was confined to the bed until within a few days of her discharge.

ANALYSIS OF THE BLOOD FOR CHOLESTERIN.—The blood presented nothing peculiar in its appearance. A quantitative analysis was made for cholesterolin, with the following result:

Quantity of blood.....	117.193 grains.
“ “ cholesterolin.....	0.108 “
Proportion of cholesterolin per 1,000 pts. of blood	0.922 “

CASE IV. CIRRHOSIS WITH ASCITES AND SLIGHT CONSTITUTIONAL DISTURBANCE.—Thomas Hughes, æt. about 33, brewer, presented himself at the Long Island College Hospital, July 1, 1862, with Dr. Dugan, of Williamsburg. He confessed that he had been in the habit of drinking more or less spirit daily for the past ten years. The abdomen began to swell about eighteen months ago. The ascites was preceded by hematemesis, when he vomited an abundance of black, clotted blood. The belly immediately began to swell and enlarged rapidly. He took hydragogues under the direction of a physician, and the dropsy disappeared, but returned whenever the medicines were discontinued. Œdema of the lower limbs occurred soon after the ascites. He has had recurrence of hematemesis twice since the first attack.

He was first tapped two or three months after the affection occurred and has been tapped about thirty times since. He was tapped last on June 27th. He is tapped and goes out the next day. He thinks nothing of it and is always for the time relieved. He has continued to drink beer daily and some spirit. After tapping his appetite is good, and food occasions no inconvenience. When the abdomen is full, food occasions a distressing distention, so that he does not eat freely.

The urine is scanty when the abdomen is full, and is free after tapping.

There is no pain in the belly or elsewhere. He is about all day but is not engaged in business. He says he is not very feeble. He presents a notably anemic aspect.

The abdomen is now moderately full (July 1). Superficial

veins of abdomen much enlarged. Heart appears not enlarged; a feeble systolic murmur over the body of the organ.

Several months before the ascites began, he got into a fracas and was badly beaten. He was not laid up, but says he did not feel well afterward and is disposed to attribute his disease thereto.

Advised to continue to tap when the abdomen refills, with tonics, hygienic measures, and abstinence from spirit, continuing the use of ale moderately. (Private records of Dr. Flint.)

July 1. A specimen of blood was taken from the arm for examination.

ANALYSIS OF THE BLOOD FOR CHOLESTERIN.—The blood was treated in the usual way, and a quantitative analysis was made for cholesterin, with the following result:

Quantity of blood.....	251.567 grains.
“ “ cholesterin.....	0.962 “
Proportion of cholesterin to 1,000 pts. of blood.	0.246 “

The following table shows the comparative quantity of cholesterin in these specimens and in the three specimens of healthy blood:

HEALTHY BLOOD			BLOOD OF CIRRHOSIS	
		Cholesterin per 1,000 pts.		Cholesterin per 1,000 pts.
Male, æt. 35.....		0.445	CASE III. Cirrhosis (se-	
“ “ 22.....		0.658	vere).....	0.922
“ “ 24.....		0.751	CASE IV. Cirrhosis (mild)	0.246
CASE III. Cirrhosis (severe).	Percentage of increase in cholesterin over minimum of healthy blood.....			107.190
	Ditto over maximum.....			22.769
CASE IV. Cirrhosis (mild).	Percentage of decrease in cholesterin below mini- mum of healthy blood...			42.469

These two cases present a very striking contrast; and the chemical examination of the blood has shown as marked a difference in the quantity of cholesterin as in the gravity of the attendant symptoms. They teach, however, an important lesson. There is not always an accumulation of cholesterin in the blood when the structure of the liver is altered, it being requisite that this alteration should involve enough of the organ to interfere with the elimination of this substance. The quantity may even fall below the natural standard in a patient who is rendered anemic by the consequences of a cirrhosis which is not sufficient to induce cholesteremia. The process of nutrition being thereby diminished in activity, the production

of this substance, by destructive assimilation, is necessarily diminished. The cholesteremia may be slight and transient; for the causes which produce it may be, to a certain extent, temporary. In Case III. the patient was confined to the bed, suffering acute pain over the region of the liver, in all probability due to a slight degree of inflammation. This interfered with the excretion of cholesterin, and its proportion in the blood was increased to 22.769 per cent. over the maximum, and 107.190 over the minimum.* As the patient was somewhat enfeebled by syphilis before the symptoms of disease of the liver made their appearance, it is probable that the quantity of cholesterin in the blood did not equal the highest standard in health. At all events, there was a notable increase even over the maximum quantity. Case IV. is not less instructive. Here is a patient who has had cirrhosis of the liver, with ascites, for eighteen months, and has been tapped more than thirty times. He apparently has suffered from nothing more than the mechanical effects of the liquid, which has interfered at times with digestion, and rendered him anemic. He is tapped and immediately relieved, going out the next day. There seems to be no interference with the functions of the liver, so far as the symptoms are concerned, other than the mechanical obstruction to the circulation; and the case, as regards symptoms, resembles cases of ovarian dropsy where the patient carries about an immense quantity of water, but suffers only from this, and is relieved temporarily when the water is removed. Considering the condition of the patient, one should not be surprised to find the cholesterin of the blood not increased, but diminished in quantity; and one may, I think, come to the conclusion from the symptoms as well as the analysis of the blood, that though the liver was affected sufficiently to produce obstruction of the circulation, there was not sufficient disease to give rise to cholesteremia.

It is evident that much more extended observations are necessary in order to establish the clinical relations of cholesteremia without jaundice; but the case of Mary Perkins shows that this condition does exist, while the case of Thomas Hughes shows that it does not follow structural

* Unfortunately the character of the stools was not noted.

TABLE OF QUANTITATIVE ANALYSES FOR CHOLESTERIN

		Quantity examined.	Cholesterin per 1,000 pts.
		grains.	
Human blood from the arm.	Healthy male æt. 35	312.083	0.445
"	" " " " æt. 22	187.843	0.658
"	" " " " æt. 24	102.680	0.751
"	" " " Simple jaundice	212.428	0.508
"	" " " Cholesteremia with jaundice	50.776	1.850
"	" " " Cirrhosis (grave)	117.193	0.922
"	" " " " (mild)	251.567	0.246
"	" " " Hemiplegia—		
	Case I. Paralyzed side.	55.458
	Sound side	128.407	0.481
	Case II. Paralyzed side.	18.381
	Sound side	66.396	0.808
	Case III. Paralyzed side.	21.824
	Sound side	52.261	0.579
Blood from carotid	179.462	0.774
" " internal jugular	} Dog experiment.	134.780	0.801
" " femoral vein		133.886	0.806
" " carotid	} Dog experiment {	140.847	0.768
" " internal jugular		97.811	0.947
" " carotid	} Dog experiment.	143.625	0.967
" " internal jugular		29.956	1.545
" " femoral vein	} Dog experiment.	45.035	1.028
" " carotid		159.537	1.257
" " portal vein	} Dog experiment.	168.257	1.009
" " hepatic vein		79.848	0.964
Human brain (subject killed instantly)		159.753	7.729
" " (Case II., killed instantly)		150.881	11.456
Human bile (specimen from Case II.)		224.583	0.618
Crystalline lens (4 lenses from the ox).		135.020	0.907
Meconium		170.541	6.245

change in the liver unless the lesion is extensive. The fact that there may be contamination of the blood by the retention of a biliary matter, without discoloration of the skin, is exceeding important; and of this there seems to me to be no doubt. A patient who has structural disease of the liver and presents symptoms of blood-poisoning is suffering from cholesteremia, although there is no icterus. The cholesteremia may vary in degree between the mildness which characterized Case III., in which it was, perhaps, temporary,* and the grave condition mentioned by Frerichs, characterized by noisy delirium and coma, and announcing a speedy fatal termination. Adding to these

* The patient having gone out of the hospital, it was impossible to settle this point.

conditions the cases of what is ordinarily called biliousness, attended with drowsiness, an indefinite feeling of malaise, constipation, etc. (and all this relieved by a simple mercurial purge, which is said to promote the secretion of the liver), is it not to be hoped that some light will be thrown on their pathology by a knowledge that there is a condition called cholesteremia! As yet this is but speculation; but the discovery of the important function of cholesterin opens a wide field of inquiry in this direction; and ere long the physician may be able to speak of "biliousness," and "liver complaint," with some definite ideas of their pathology.

The table on page 235 gives the results of the quantitative analyses for cholesterin which have been referred to in this article.

CONCLUSIONS

The observations contained in the preceding article seem to me to justify the following conclusions:

1. Cholesterin exists in the bile, the blood, the nervous matter, the crystalline lens and the meconium, but does not exist in the feces under ordinary conditions. The quantity of cholesterin in the blood of the arm is five to eight times more than the ordinary estimate.

2. Cholesterin is formed, in great part if not entirely, in the substance of the nervous matter, where it exists in great abundance, from which it is taken up by the blood and constitutes one of the most important of the effete or excrementitious products of the body. Its formation is constant, and it always exists in the nervous matter and the circulating fluid.

3. Cholesterin is separated from the blood by the liver, appears as a constant constituent of the bile and is discharged into the alimentary canal. The history of this substance, in the circulating fluid and in the bile, marks it as a product destined to be discharged from the body, as an excretion. It preëxists in the blood, subserves no useful purpose in the economy, is separated by and not formed in the liver, and if this separation is interfered with, it accumulates in the system.

4. The bile has two separate and distinct functions dependent on the presence of two constituents of entirely

different characters. It has a function connected with nutrition. This is dependent on the presence of the glycocholate and taurocholate of soda, which do not preëxist in the blood, subserve a useful purpose in the economy and are not discharged from the body, are found in the liver and peculiar to the bile, do not accumulate in the blood when the function of the liver is interfered with, and are, in short, products of secretion. The bile has another function connected with depuration, which is dependent on the presence of cholesterin, which is an excretion. The flow of the bile is remittent, being much increased during the digestive act, but produced during the intervals of digestion for the purpose of separating cholesterin from the blood.

5. The ordinary normal feces do not contain cholesterin, but contain stercorin—formerly called serolin, from its being supposed to exist only in the serum of the blood. Stercorin results from a transformation of the cholesterin of the bile during the digestive act.

6. The change of cholesterin into stercorin does not take place when digestion is arrested or before this process begins; consequently, stercorin is not found in the meconium or in the feces of hibernating animals during their torpid condition. These matters contain cholesterin in large abundance, which also sometimes appears in the feces of animals after a prolonged fast. Stercorin is the form in which cholesterin is discharged from the body.

7. The difference between the two familiar varieties of jaundice, one characterized only by yellowness of the skin and comparatively innocuous, while the other is attended with very grave symptoms and is almost invariably fatal, is dependent upon the obstruction of the bile in one case and its suppression in the other. In the first instance, the bile is confined in the excretory passages and its coloring matter is absorbed; while in the other, cholesterin is retained in the blood.

8. There is a condition of the blood dependent upon the accumulation of cholesterin which I have called cholesteremia. This occurs only when there is structural change in the liver, which incapacitates it from performing its excretory function. It is characterized by symptoms of a grave character, referable to the brain, and probably is

dependent upon the effects of the retained cholesterin on this organ. It occurs with or without jaundice.

9. Cholesteremia does not occur in all cases of structural disease of the liver. Enough of the liver must be destroyed to prevent the due elimination of cholesterin. In cases in which the organ is but moderately affected, the sound portion is capable of performing the eliminative function of the whole.

10. In cases of simple jaundice, when the feces are decolorized and the bile is entirely shut off from the intestine, stercorin is not found in the evacuations; but in cases of jaundice with cholesteremia, stercorin may be found, though always very much diminished in quantity, showing that there is an insufficiency in the separation of the cholesterin from the blood, although its excretion is not entirely suspended. After death, but a small quantity of bile is found in the gall-bladder.

PLATE I

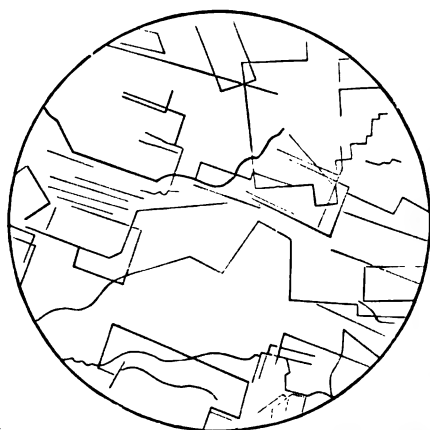


FIG. 1.

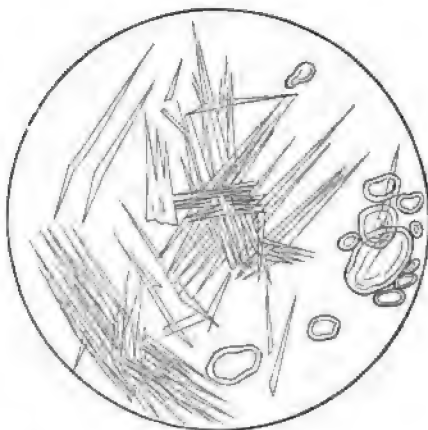


FIG. 2.

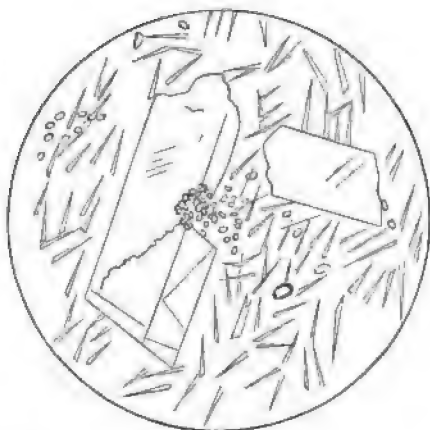


FIG. 3.

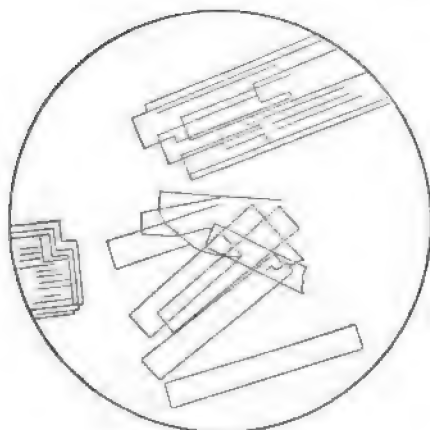


FIG. 4.

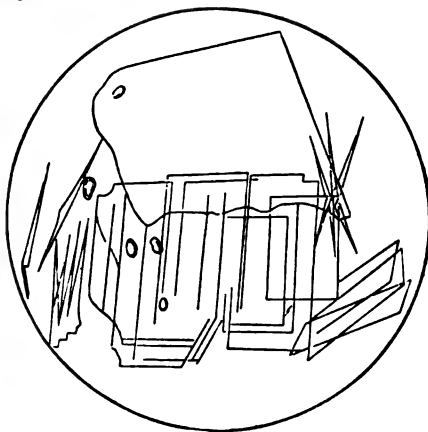


FIG. 5.

PLATE II.

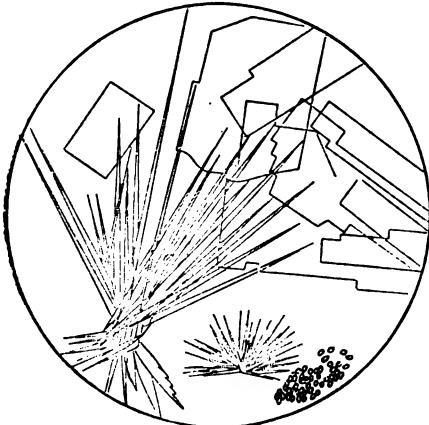


FIG. 6.

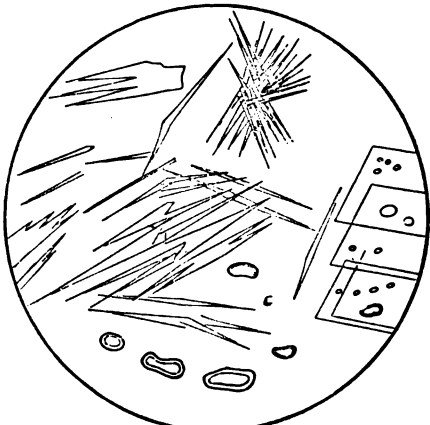


FIG. 7.

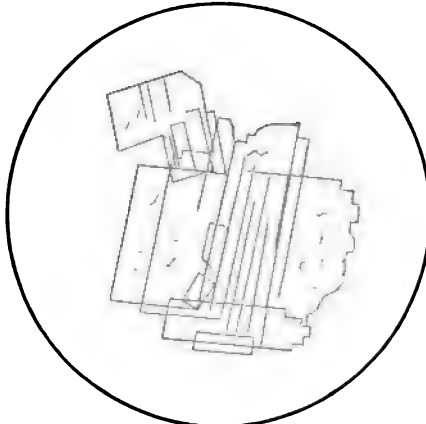


FIG. 8.

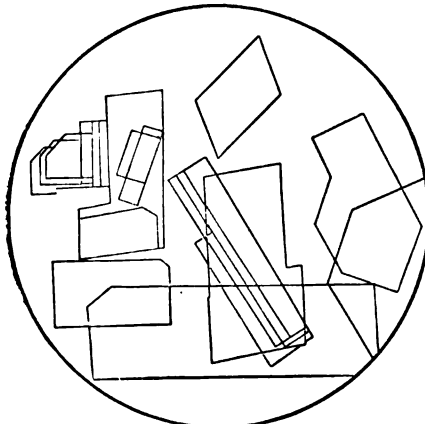


FIG. 9.

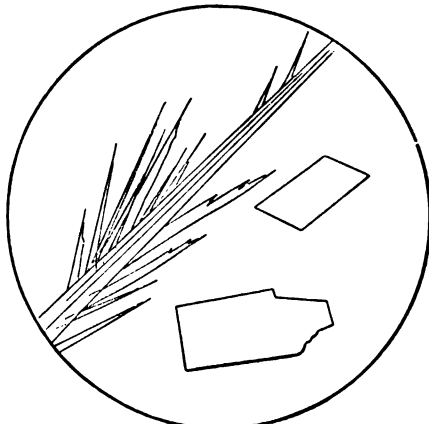


FIG. 10.

PLATE III

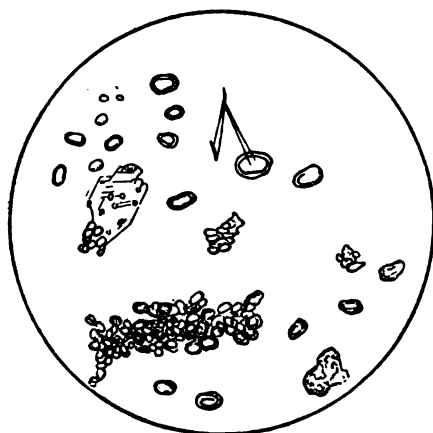


FIG. 11.

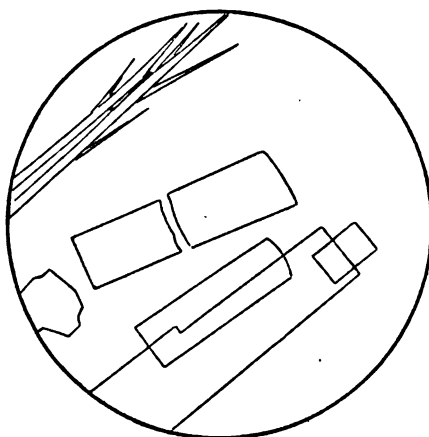


FIG. 12.

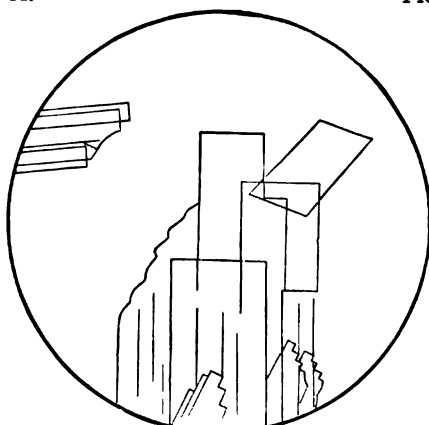


FIG. 13.

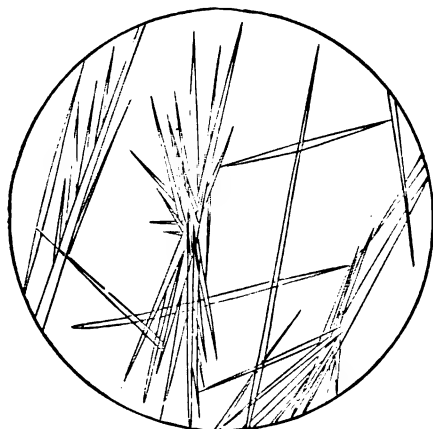


FIG. 14.

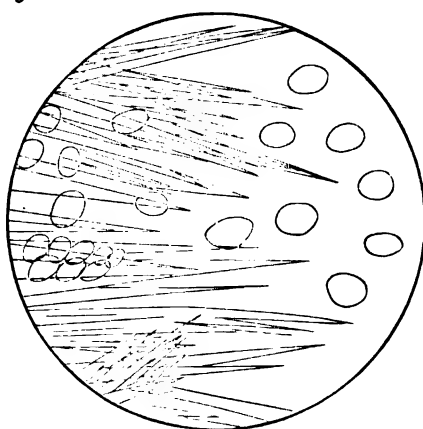


FIG. 15.

EXPLANATION OF THE PLATES

- FIG. 1.—Cholesterin extracted from meconium. $\frac{1}{8}$ inch objective.
- FIG. 2.—Stercorin and fatty matters from the blood of the carotid artery. $\frac{1}{8}$ inch objective.
- FIG. 3.—Cholesterin and small broken crystals of stercorin from the same specimen of blood from the carotid, examined eleven days after. Nachet, No. 3 objective.
- FIG. 4.—Cholesterin from the brain. $\frac{1}{8}$ inch objective.
- FIG. 5.—Cholesterin from the blood of the internal jugular, with a few needles of stercorin. $\frac{1}{8}$ inch objective.
- FIG. 6.—Cholesterin and stercorin from the same extract as Fig. 5, examined the next day. $\frac{1}{8}$ inch objective.
- FIG. 7.—Cholesterin and stercorin from the blood of the vena cava. $\frac{1}{8}$ inch objective.
- FIG. 8.—Cholesterin from the blood of the portal vein. $\frac{1}{8}$ inch objective.
- FIG. 9.—Cholesterin from the blood of the hepatic artery. $\frac{1}{8}$ inch objective.
- FIG. 10.—Cholesterin and stercorin from the blood of the hepatic artery. $\frac{1}{8}$ inch objective.
- FIG. 11.—Fatty substances from the blood of the hepatic vein. $\frac{1}{8}$ inch objective.
- FIG. 12.—Cholesterin and stercorin from the same specimen, examined the following day. $\frac{1}{8}$ inch objective.
- FIG. 13.—Cholesterin extracted from bile. $\frac{1}{8}$ inch objective.
- FIG. 14.—Stercorin from human feces. $\frac{1}{8}$ inch objective.
- FIG. 15.—Stercorin from the same specimen, after it had been melted, placed on a glass slide, covered with thin glass, and allowed to crystallize. The crystallization was very slow, occupying some weeks. This Fig. shows splitting of the borders and points of the crystals with the globules referred to on page 207. The globules were of variable size, and some of them were arranged in rows, which, with an inferior microscope, might be mistaken for varicosities on the needles. From their appearance in this specimen, after it had been thoroughly purified, I am inclined to change the opinion expressed on page 207, and regard them as composed of stercorin and not fatty impurities. $\frac{1}{8}$ inch objective.

X

THE EXCRETORY FUNCTION OF THE LIVER

Published in the "Transactions of the International Medical Congress," held in Philadelphia in September, 1876.

I HAVE selected as the subject which I shall have the honor to present to the Section on Biology, the Excretory Function of the Liver, for the reason that it seemed to me better to discuss a question concerning which I had made personal and original investigations than to recite the observations of others, however interesting and important the latter might be. I have ventured to assume that the views which I have to offer are not without importance; and they are certainly not so familiar as many other topics which I might with propriety have selected. I shall, therefore, endeavor to bring to your notice, in the simplest manner possible, what I have myself learned in regard to the liver as an organ of excretion.

It is now well known that the liver has a variety of important functions with which physiologists are more or less acquainted. The liver produces a substance which is converted into sugar and is carried away in the torrent of the circulation. It secretes bile which performs an important office in digestion. In addition to the digestive function of the bile, I think I have shown that this fluid serves as the vehicle for the elimination of at least one excrementitious matter, which is discharged in a modified form in the feces. If the liver serves as an organ of excretion, it is evidently of great importance, from a pathological as well as a physiological point of view, to arrive at an accurate knowledge of the mechanism of this function. For a long time, many pathological conditions have been attributed to defective or perverted action of the liver; but the terms, "liver complaint," "biliousness," etc., have failed to convey any definite pathological idea, and it is

probably true that the liver has been accused of many sins of omission and commission without any positive scientific reason. Many medical writers have assumed, in an indefinite way, that the liver possesses an excretory function; but so far as I know, no physiologist has described any definite excrementitious substance eliminated by this organ prior to my observations in 1862.

There are certain general laws applicable to secretions and to excretions, which it is important to consider in discussing the functions of the bile:

I. Secretions have some useful purpose to serve in the economy, and as a rule they are not discharged from the body in health. Excretions have no function in the economy and are discharged from the body.

II. The flow of secretions from the glands usually is intermittent, occurring when their function is called into action. The flow of excretions usually is either constant or remittent.

III. The production of excretions depends upon the general process of disassimilation, which is constant. The production of secretions has no relation to disassimilation, but is connected with processes which usually take place at intervals.

IV. The elements of secretion, which give to secreted fluids their characteristic physiological properties, are formed *de novo* in the glands themselves out of materials furnished by the blood, and they do not preëxist ready-formed in the circulating fluid. The elements of excretion preëxist in the blood, being taken up by the lymph or by the blood from the tissues, and they are separated from the blood by organs which have no part in their actual production; except that excrementitious substances may be changed one into another, as creatin into creatinin or uric acid into urea.

V. When secreting organs are removed or destroyed, there is no vicarious production of the peculiar constituents of the secretions; these elements do not accumulate in the blood; and the system suffers simply from the absence of the function of the special secretion. When excreting organs are removed or destroyed, there may be a vicarious elimination of the excrementitious matters by other organs or the system may suffer toxic effects from

the accumulation of excrementitious matters in the circulating fluid.

VI. The characteristic constituents of true secretions generally are reabsorbed by the blood; but they are taken up in a modified form, so that they are not to be recognized in the circulating fluid. Elements of excretion are with difficulty reabsorbed by the blood after they have once been separated by the proper organs.

The applications of the foregoing general laws may be readily made to the pancreatic juice as contrasted with the urine, which two fluids may be taken as types respectively of secretions and of excretions. Before making an application of these laws to the bile, we may consider the simple question as to whether it can be shown that this fluid has a useful function to perform as a secretion. If the bile has no such function, an animal would live and maintain its normal condition when the bile is diverted from the intestine and discharged from the body. This question has been made the subject of experimental observation by simply cutting off the bile-duct and making a fistula into the gall-bladder, by which the bile is discharged. The operative procedure involved is not difficult, but is very likely to be followed by fatal peritonitis, so that few experiments of this kind have succeeded. In the experiments which have succeeded, in the hands of Schwann, Bidder and Schmidt, Nasse, Bernard and myself, the dogs have lived for thirty or forty days, dying with all the symptoms of inanition. In one remarkably successful experiment performed by myself, the dog lived for thirty-eight days, had a voracious appetite and died at the end of that period after having lost about four-tenths of his weight. In this experiment the bile-duct was ligatured in two places and the intermediate portion was exsected. A fistula was then made into the fundus of the gall-bladder, which was kept open. The animal ate well on the day of the operation, and there was very little peritonitis. The only observation in which contrary results were obtained is one made by Blondlot.* In this case a fistula was made into the gall-bladder after the bile-duct had been divided. The animal

* Blondlot, "Essai sur les fonctions du foie et de ses annexes," Paris, 1840, p. 55 *et seq.*; and "Inutilité de la bile dans la digestion," Paris, 1851.

lived for five years, and after fifteen days following the operation, was in good flesh and apparently suffered no inconvenience from the discharge of the bile from the fistula. During the first fifteen days the animal licked the bile from the fistula, but this was afterward prevented by a muzzle. After a time he made no attempt to lick the bile. Blondlot attributed the emaciation which occurred during the first fifteen days to this licking of the bile. When the animal died, more than five years after the operation, an examination of the parts was made in the presence of several physicians and students of medicine and no communication could be found between the bile-duct and the intestine. From this observation Blondlot concluded that the bile had no function in digestion and that it was a purely excrementitious fluid; and he assumed that the cause of death in other experiments of a similar kind was the licking of the bile as it flowed from the fistula. In my own case of biliary fistula, in which the dog died after thirty-eight days, the animal was prevented by a muzzle from licking the bile.

The only point to consider, as it seems to me, in this single experiment of Blondlot, is whether or not a communication had been reëstablished between the bile-duct and the intestine. If such a communication existed, it would be easy to explain the survival of the animal. The following experiment, which I undertook for a different purpose, satisfied me upon this point:

I attempted to estimate in a dog the entire quantity of bile discharged in the twenty-four hours. With this object in view, I cut down upon the bile-duct, emptied the gall-bladder, secured a canula in the duct and attached a rubber-bag to the canula for the purpose of collecting the bile. Twenty-three hours after the operation the bag was in place and nearly full of bile. Just before the end of the twenty-four hours, however, the animal ruptured the bag, and the experiment, so far as its original object was concerned, was a failure. I then simply pulled the canula from the wound and set the animal at liberty. In about four weeks, after the wound had closed and the feces had become of normal color, the animal, when in a perfectly normal condition, was killed and the parts were carefully examined in the presence of several assistants. It is well

known that in dogs ducts that have been divided have a remarkable tendency to become reestablished. In this case, inasmuch as no bile was discharged externally and the feces were of normal color, it was certain that the bile was discharged into the intestine. Nevertheless I searched for more than an hour for the communication before it was discovered. The only reasonable way, as it appears to me, to reconcile the single experiment of Blondlot with those of other observers is to suppose that in his observation a communication between the bile-duct and the intestine had become established, which he failed to find. The difficulty which I experienced in finding the communication in my own observation led me to conclude that a communication existed in the case reported by Blondlot, which he did not discover.

It is in accordance with my own observations, as well as with those of other physiologists, to conclude that the bile is a secretion, and that it has a function to perform in connection with the digestive process, which function is essential to life.

Assuming that the bile has an important and an essential office in digestion, is it not possible that it may also serve the purpose of elimination, and contain elements of excretion! This is a view which has not been advanced by physiologists, who have regarded the bile either as a secretion or an excretion and have not imagined that it could serve both functions. Before I take up the experimental facts bearing upon this question, I propose to consider the arguments to be drawn from a study of the composition of the bile and its discharge into the intestine. It was this idea which first led me to investigate the physiological relations of cholesterin.

The bile certainly has an important function as a secretion; and its flow, although not intermittent, is more abundant during the process of intestinal digestion. The peculiar biliary salts, the glycocholate and the taurocholate of soda, are formed in the liver and do not preëxist in the blood. When the structure of the liver is invaded by disease so as to interfere with the production of bile, the biliary salts do not accumulate in the blood. The biliary salts are reabsorbed in a modified form in the intestine; for the quantity of one of their elements (sulphur) found

in the feces is very much less than the quantity discharged into the intestine.

On the other hand, in regard to one constant constituent of the bile (cholesterin), it is not known to have any function in connection with digestion. The secretion of bile is continuous, although its flow is increased during digestion. Cholesterin, while it is an invariable constituent of the bile, exists in the blood and in certain of the tissues of the body.

The questions to determine experimentally in regard to cholesterin are the following:

Is cholesterin produced in any of the tissues of the body?

Is cholesterin separated from the blood by the liver?

When the liver undergoes structural change in disease, does cholesterin accumulate in the blood?

Is cholesterin reabsorbed in the intestine or is it discharged, either unchanged or in a modified form, in the feces?

These are the questions which I endeavored to answer by a series of experimental investigations, made in the spring of 1862, and published in October of the same year, in the "American Journal of the Medical Sciences."

PROCESS FOR THE ESTIMATION OF CHOLESTERIN IN THE BLOOD.—The following is the process which I fixed upon, after a number of trials, for the quantitative analysis of the blood for cholesterin: The entire blood, serum and clot, is evaporated to dryness. The dry residue is then pulverized in an agate mortar and treated for twelve to twenty-four hours with ether, in the proportion of about one fluidounce of ether to one hundred grains of the original weight of blood. This is filtered, and the ethereal extract, which contains cholesterin and fats, is evaporated. The residue of this evaporation is then extracted with boiling alcohol, in the proportion of one fluidrachm for one hundred grains of the original weight of blood. This extract is filtered while hot and the filtrate is evaporated, leaving the cholesterin and a certain quantity of saponifiable fats. To remove the saponifiable fats, add to the residue a weak solution of potash, and allow it to remain for about two hours; then dilute with water, filter, and

wash the filter with water until the liquid which passes through becomes neutral. Dry the filter; wash it with ether; evaporate the ether; extract the residue with hot alcohol as before; evaporate the alcoholic extract, and the residue will consist of cholesterin, perfectly pure, as can be determined by means of the microscope. Using this process for the determination of cholesterin, a number of observations were made upon dogs, from which I select the following as typical, the results having been repeatedly confirmed:

OBSERVATION I. EXPERIMENT SHOWING AN INCREASE IN CHOLESTERIN IN THE BLOOD PASSING THROUGH THE BRAIN. (The dog was not etherized.)

Blood from the carotid, 140.847 grains, contained 0.108 grain of cholesterin, or 0.768 part of cholesterin per 1,000.

Blood from the internal jugular, 97.811 grains, contained 0.092 grain of cholesterin, or 0.947 part of cholesterin per 1,000.

The increase in the proportion of cholesterin in the blood in passing through the brain was 23.309 per cent.

This observation, which was frequently repeated with the same general result, seems to show that the blood gains cholesterin in its passage through the brain. It is well known that cholesterin is always present in nervous substance, not in a crystallized form, but in a condition of molecular union with nitrogenous and other matters. In order to verify this fact, I examined the brains of two subjects who had been killed instantly by accident while in perfect health, in one case finding a proportion of cholesterin of 7.729 parts per 1,000, and in the other, 11.456 parts per 1,000.

The experiment just described was made with a view of determining whether or not the brain gives up cholesterin to the blood as it circulates through this organ; and the following experiment was made to determine whether the venous blood of other parts contains an excess of cholesterin. Theoretically, the blood of the femoral vein should contain a little more cholesterin than arterial blood, this excess being derived from the nerves of the extremity, although the increase would probably be not so great as in the blood of the internal jugular, which comes almost exclusively from the great nervous centre.

OBSERVATION II. EXPERIMENT SHOWING AN EXCESS OF CHOLESTERIN IN THE BLOOD OF THE INTERNAL JUGULAR AND FEMORAL VEINS OVER THE ARTERIAL BLOOD. (The dog was not etherized.)

Blood from the carotid, 143.625 grains, contained 0.679 grain of cholesterin, or 0.967 part of cholesterin per 1,000.

Blood from the internal jugular, 29.956 grains, contained 0.046 grain of cholesterin, or 1.545 part per 1,000.

Blood from the femoral vein, 45.035 grains, contained 0.046 grain of cholesterin, or 1.028 part per 1,000.

The increase in the proportion of cholesterin in the blood in passing through the brain was 59.772 per cent.

The increase in the proportion of cholesterin in the blood in passing through the lower extremity was 6.308 per cent.

This experiment confirms the previous observation upon the increase of cholesterin in the blood in passing through the brain, and it shows, in addition, that the blood gains cholesterin in other parts. Inasmuch as the nervous tissue is the only tissue in the extremities which contains cholesterin, it is probable that the excess contained in the blood of the femoral vein over the arterial blood was derived from the nerves.

It occurred to me that cases of old hemiplegia would present favorable conditions for verifying in the human subject the observations made on the lower animals. It has been ascertained that when the function of nerves is permanently abolished they soon become degenerated and their nutrition is modified; and it seems probable that if cholesterin is one of their important products of disassimilation, the quantity of cholesterin in the blood from paralyzed parts should be very small. Taking the blood, for example, from the paralyzed arm of a hemiplegic, this blood, coming from paralyzed parts, should contain less cholesterin than the blood from the sound arm. Of course, the blood from the arm contains no blood which has passed through the brain, which is assumed to be sound upon the paralyzed side. I examined, therefore, the blood from both arms in three cases of hemiplegia in the Charity Hospital on Blackwell's Island:

CASE I.—Sarah Rumsby, æt. 47, is affected with hemiplegia of the left side. Two years ago she was taken with apoplexy and was insensible for three days. When she recovered consciousness she found herself paralyzed on the left side. She says she had epilepsy four or five years before the attack of apoplexy. She has now

complete paralysis of motion on the affected side, with the exception of some slight power over the fingers. Sensation is not affected. The speech is perfect and her general health is good.

CASE II.—Anna Wilson, æt. 23, is affected with hemiplegia of the right side. Four months ago she became unconscious and recovered in one day, with loss of motion and sensation on the right side. She is now improving and can use the right arm slightly. The leg is not so much improved because she will make no effort to use it.

CASE III.—Honora Sullivan, æt. 40, is affected with hemiplegia of the right side. About six months ago she became unconscious, recovering the next day, with paralysis. The leg was less affected than the arm from the first. Her condition is about stationary as regards the arm but the leg has somewhat improved.

A small quantity of blood was drawn from either arm in these three cases. In each instance it was drawn from the paralyzed side with difficulty and but a small quantity could be obtained.

The specimens were all examined for cholesterin, with the following results:

OBSERVATION III. QUANTITIES OF CHOLESTERIN IN THE BLOOD OF THE PARALYZED AND THE SOUND SIDES IN THREE CASES OF HEMIPLEGIA

CASES.	Blood.	Cholesterin.	Cholesterin per 1,000 parts.
	grains.	grains.	
Case I. Paralyzed side....	55.458	The watch-glass contained 0.031 grain of substance, but the most careful examination with the microscope failed to show crystals of cholesterin.
Sound side.....	128.407	0.062	0.481.
Case II. Paralyzed side....	18.381	Same as in Case I.
Sound side.....	66.396	0.062	0.808.
Case III. Paralyzed side....	21.842	Same as in Case I.
Sound side.....	52.261	0.031	0.579.

The conclusion from the experiments upon dogs and the three observations upon the human subject is inevitable, that cholesterin is produced in the substance of the brain and in the nervous tissue generally, as this substance is not contained in the muscular tissue or in any other parts except the crystalline lens, the liver and the spleen. The question now to determine is the relation of cholesterin to the nervous system. Is it one of the products of disassimilation of its tissue? If this is the fact, cholesterin is an excrementitious product and it must be sepa-

rated from the blood by some organ or organs and discharged from the body. Inasmuch as the bile always contains cholesterolin, we naturally look to the liver as the organ for its elimination; for it is not found in the secretion of any other gland.

I employed essentially the same method in studying the question of the elimination of cholesterolin as that used in determining the seat of its production, analyzing the blood going to and coming from the liver. Upon this point I made a number of observations, the general results of which were invariable. The following experiment is a type of these observations:

OBSERVATION IV. EXPERIMENT SHOWING THAT CHOLESTERIN IS SEPARATED FROM THE BLOOD IN ITS PASSAGE THROUGH THE LIVER. (The dog was etherized.)

Arterial blood, 159.537 grains, contained 0.200 grain of cholesterolin, or 1.257 part of cholesterolin per 1,000.

Blood of portal vein, 168.257 grains, contained 0.170 grain of cholesterolin, or 1.009 part of cholesterolin per 1,000.

Blood of hepatic vein, 79.848 grains, contained 0.077 grain of cholesterolin, or 0.964 part of cholesterolin per 1,000.

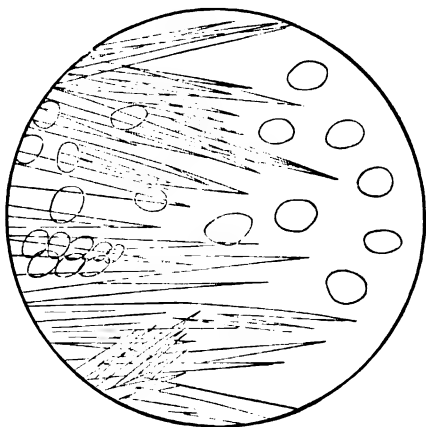
The loss in the proportion of cholesterolin in arterial blood in passing through the liver was 23.309 per cent.

The loss in the proportion of cholesterolin in the portal blood in passing through the liver was 4.460 per cent.

The bile always contains a certain proportion of cholesterolin, which I found, in a specimen taken from the gall-bladder of a subject who had been killed instantly while in perfect health, to be 0.618 part per 1,000. As I have demonstrated that the blood gains cholesterolin in its passage through the brain and probably also from the general nervous tissue, that cholesterolin is separated from the blood in its passage through the liver, and that cholesterolin is invariably found in the bile and is discharged into the intestine, it seems to be proved that one of the functions of the liver is to eliminate this substance. If it can be shown that the cholesterolin thus separated from the blood by the liver is discharged from the body, the fact that it is apparently produced in the nervous tissue and is taken up by the blood would point strongly to the conclusion that cholesterolin is an excrementitious matter and is one of the products of disassimilation of the nervous tissue.

STERCORIN.—I made repeated examinations of the normal feces, with the view of determining the presence of cholesterin and its quantity. Although it is often stated by authors that cholesterin exists in the feces, I was unable to find it after the most careful examination; and I subsequently failed to discover any writer who had actually extracted it from the normal dejections. The process which I employed was essentially the same as that used in examinations of the blood, except that the extracts were decolorized by filtering through animal charcoal, and the alcoholic extract was treated with potash for one or two hours at nearly the boiling point. Treated in this way, the feces gave an extract which was non-saponifiable but which did not crystallize for several days. After a few days, delicate, needle-shaped crystals began to appear, gradually increasing in number and breadth, and as they became broader, becoming split at the points and edges. These crystals presented all the characters of the crystals of a substance extracted from the serum of the blood by Boudet, in 1833 ("Annales de chimie et de physique"), which he called "séroline." In some of my earlier ob-

servations upon the blood, I obtained these crystals; but I came to the conclusion that the so-called séroline was not a normal constituent of the blood but was formed during the process used for the extraction of cholesterin. With this view, finding the so-called séroline to be a constant constituent of the normal feces, I called the substance stercorin, regarding it as one of the excre-



Stercorin from normal human feces ($\frac{1}{16}$ inch objective).

mentitious constituents of fecal matter. Crystals of stercorin are shown in the accompanying figure. The round-drops probably are composed of the same substance, as

they disappear when the crystallization is complete. The idea that these crystals obtained from blood result from the transformation of cholesterin is strengthened by the fact that the cholesterin of the bile is changed into stercorin in its passage through the alimentary canal. Stercorin, like cholesterin, is soluble in ether, very soluble in hot alcohol and strikes a red color with strong sulphuric acid.

I obtained from the feces of the twenty-four hours of a perfectly healthy man 10.417 grains of stercorin. It is estimated by Dalton that the total quantity of bile in twenty-four hours is 16,940.00 grains, and the total quantity of cholesterin, according to my estimate of 0.618 parts per 1,000, is 10.469 grains, giving a difference between the estimated quantity of cholesterin and the actual quantity of stercorin extracted from the feces of only 0.052 of a grain. This sustains the idea of the change of the cholesterin of the bile into the stercorin of the feces.

Observations made by myself and others seem to show that the change of cholesterin into stercorin is incidental to the process of digestion. Cholesterin is found in quantity in the feces of hibernating animals and in the meconium, when, of course, there is no intestinal digestion, but when the bile is none the less discharged into the alimentary canal. I made an examination of human meconium and found cholesterin in the proportion of 6.245 parts per 1,000 and no stercorin. I examined the human feces in a case of simple jaundice from obstruction of the bile-duct, the feces being clay-colored, and found neither cholesterin nor stercorin. Nineteen days after, when the jaundice had disappeared and the color of the feces was normal, I found stercorin and no cholesterin. In the feces of a dog which had been deprived of food for forty-eight hours, I found stercorin and a small quantity of cholesterin. So far as can be learned from these facts and observations, then, it seems that the cholesterin of the bile is discharged in the feces unchanged when no digestion takes place, but that it is discharged in the form of stercorin under the ordinary and normal conditions of the digestive process.

PATHOLOGICAL RELATIONS OF CHOLESTERIN.—CHOLESTEREMIA.—A knowledge of the relations of urea to nutrition bears so directly upon the pathology of renal dis-

eases, that the pathological relations of any newly-discovered excrementitious matter assumes at once the greatest importance. If it is true that cholesterin, like urea, is a product of disassimilation, and that it is eliminated by the liver as urea is eliminated by the kidneys, one would expect to find, in cases of serious structural disease of the liver, an accumulation of cholesterin in the blood, or cholesteremia, as uremia exists in certain stages of extensive organic disease of the kidneys. It has long been observed, indeed, that although simple jaundice due to resorption of the coloring matter of the bile usually is a trivial affection, there are cases of extensive change in the structure of the liver in which there is apparently a toxic condition dependent upon the presence of some excrementitious or poisonous substance in the blood. Pathologists have examined the blood in such cases with the view of ascertaining the nature of the supposed poisonous matter. Frerichs and others repeatedly examined the blood in cases of grave jaundice, expecting to discover the biliary salts or acids, but they never detected any substance which would react with Pettenkofer's test.* Becquerel and Rodier examined the blood in a case of jaundice and found "cholesterin excessively abundant," but they did not recognize the significance of this fact.† In such cases pathologists have looked for the biliary acids and their derivatives and not for cholesterin. In order to throw some light upon the pathology of grave jaundice, Müller,‡ Kunde,* Lehmann,|| and Moleschott^ have extirpated the liver in frogs and kept the animals alive for several days, or even two or three weeks. On examining the blood, these physiologists failed to discover the biliary salts. They made no analyses of the blood for cholesterin. I hope to be able to show conclusively, by observations upon cases of disease of the liver in the human subject, that there may be an accumulation of cholesterin in the blood, or cholesteremia, and that this occurs in certain cases of serious structural disease of the liver.

* Frerichs, "Diseases of the Liver," London, 1860, vol. i., p. 95.

† Becquerel et Rodier, "Traité de chimie pathologique," Paris, 1854, p. 210.

‡ Müller, "Manuel de physiologie," Paris, 1851, tome i., p. 122.

* Kunde, "De Hepatis Extirpatione," Berolini, 1850.

|| Lehmann, "Physiological Chemistry," Philadelphia, 1855, vol. i., p. 476.

^ Moleschott, "Comptes rendus," Paris, 1855, tome xl., p. 1040.

In cases of simple jaundice there is resorption of the coloring matter of the bile from the excretory passages.

In cases of grave jaundice, which almost invariably terminate fatally, there is cholesteremia, or accumulation of cholesterin in the blood.

There are cases of structural disease of the liver in which there is no jaundice, but nevertheless there is cholesteremia.

In the following cases, having first determined the proportion of cholesterin in normal blood, I examined the blood for cholesterin with reference to the points just stated:

OBSERVATION V. PROPORTION OF CHOLESTERIN IN NORMAL BLOOD.—

Male, æt. 35	0.445	part of cholesterin per 1,000.
“ “ 22	0.658	“ “ “
“ “ 24	0.751	“ “ “

OBSERVATION VI. CASE OF JAUNDICE DEPENDENT PROBABLY UPON DUODENITIS.—This case presented the symptoms of simple jaundice from temporary obstruction of the bile-duct. June 21, 1862, 212.428 grains of blood were taken from the arm. The proportion of cholesterin per 1,000 was 0.508, which is within the limits of health, according to the results obtained in my examinations of normal blood. The feces, which were clay-colored, were examined, and I found neither cholesterin nor stercorin. July 11, the patient had entirely recovered; there was no jaundice, and the feces had become normal.

OBSERVATION VII. CASE OF GRAVE JAUNDICE WITH CIRRHOSIS.—This case presented intense jaundice, ascites, great general prostration, and toward the close of life, symptoms of blood-poisoning. The patient was admitted to the Charity Hospital on Blackwell's Island, June 16, 1862. On June 21 50.776 grains of blood were taken from the arm. This blood contained a proportion of 1.850 part of cholesterin per 1,000, an increase of 146.338 per cent. over the maximum quantity obtained from normal blood. The patient died June 27, 1862. There was double vision six days before death and stupor for the last three or four days. The liver, examined after death, was in a condition of cirrhosis. The gall-bladder was contracted and contained but about two drachms of bile. The fibrous substance of the liver was increased in quantity and the liver-cells were shrunken. The feces were taken a few days before death. The amount was small, only 272.1 grains in twenty-four hours, and contained 0.077 of a grain of stercorin. I found 10.417 grains of stercorin in the feces of the twenty-four hours in a healthy male.

OBSERVATION VIII. CASE OF CIRRHOSIS WITH ASCITES AND CONSIDERABLE AFFECTION OF THE GENERAL HEALTH.—In this case

there was general prostration confining the patient to the bed. After a tapping, the liver was explored and found to be considerably diminished in size; 117.193 grains of blood were taken from the arm, containing a proportion of 0.922 of a part of cholesterin per 1,000, an increase of 22.769 per cent. over the maximum proportion obtained in my examinations of normal blood. In this case there were no nervous symptoms.

OBSERVATION IX. CASE OF CIRRHOSIS WITH ASCITES AND SLIGHT CONSTITUTIONAL DISTURBANCE.—This patient had suffered from ascites for eighteen months and had been tapped about thirty times. He is immediately relieved by tapping and goes out the next day. July 1, 1862, 251.567 grains of blood were taken from the arm, which gave a proportion of cholesterin of 0.246 of a part per 1,000, or 44.719 per cent. less than the minimum obtained in my examinations of normal blood.

The cases just detailed, taken in connection with my observations upon animals, are certainly very striking. In the case of simple jaundice, which recovered, the proportion of cholesterin in the blood was within the limits of health. In the case of ascites, the patient not suffering much disturbance, the proportion of cholesterin in the blood was considerably below the normal standard. In the case of grave jaundice, which terminated fatally with symptoms of serious disturbance of the nervous system, the proportion of cholesterin in the blood was enormously increased, being nearly three times greater than the maximum obtained in my examinations of normal blood. In the case of cirrhosis with considerable affection of the general health, the proportion of cholesterin in the blood was considerably above the maximum obtained in my examinations of normal blood.

LITERATURE BEARING UPON THE "NEW EXCRETORY FUNCTION OF THE LIVER," SINCE THE PUBLICATION OF MY OBSERVATIONS IN 1862

October, 1862.—My researches were published in the "American Journal of the Medical Sciences."

1868.—A translation of my memoir into French was published in Paris and presented to the Academy of Sciences for the Monthyon prize.

1869.—The commission from the French Academy of Sciences reported upon my observations and awarded an "honorable mention" with a "recompense" of fifteen hundred francs.

1869.—Grollemund ("Thèse de Strasbourg") made observations upon the injection of the biliary salts into the blood in large quantity in dogs, and noted certain disturbances of the nervous system.

1869.—Tincelin ("Thèse de Strasbourg") made observations in which he failed to obtain any marked nervous disturbances following the injection of the biliary salts into the blood in dogs.

1869.—Pagès ("Thèse de Strasbourg") injected the bile-duct in dogs with a solution of sulphate of iron, which he thought destroyed the epithelium of the liver and interfered with its eliminative function, producing accumulation of cholesterin in the blood.

1870.—Feltz and Ritter ("Journal de l'anatomie," Paris, 1870) confirmed the results obtained by Pagès with the sulphate of iron. They found no marked effects following the injection of the biliary salts, taurin or glycochol into the veins. They also injected cholesterin in soap and water. The cholesterin was not dissolved, and masses of cholesterin were found in the small pulmonary vessels, producing death by embolism.

1872.—Picot ("Journal de l'anatomie," Paris, 1872) noted an accumulation of cholesterin in the blood in a case of acute yellow atrophy of the liver which terminated fatally. He found a proportion of cholesterin in the blood in this case of 1.804 part per 1,000, more than double the maximum which I obtained in examinations of normal blood.

1873.—Koloman Müller ("Archiv für experimentelle Pathologie und Pharmakologie," Leipzig, 1873) made an elaborate series of experiments upon dogs. No serious or marked results followed the injection of the biliary salts or taurin into the blood. He rubbed cholesterin with glycerin and made a solution in soap and water. He injected 2.16 fluidounces of this solution, containing about 69 grains of cholesterin, into the veins. In five experiments he produced "a complete picture of the symptoms of grave jaundice."

CONCLUSIONS OF KOLOMAN MÜLLER.—"It appears to me to be certain that those cerebral symptoms which accompany severe jaundice and many diseases of the liver, the general manifestations of which have been called 'cholemic intoxication,' are produced by an abnormal accumulation of cholesterin in the blood. This accumulation of cholesterin is contingent upon that alteration of the tissue of the liver, which, in such cases, it suffers more or less."

1875 and 1876.—Feltz and Ritter ("Journal de l'anatomie," Paris, 1875 and 1876) in opposition to their former experiments, conclude that the biliary salts injected into the blood produce grave changes, mainly in the blood corpuscles. The corpuscles become diffuent, change their form, the hemoglobin transudes and crystallizes, and the power of absorption of oxygen progressively diminishes.

The general results of observations bearing upon the physiological relations of cholesterin, made since 1862, are confirmatory of my observations. As regards cholestere-mia, the experiments of Müller are the most important. Indeed, they supply the only missing link in my chain of experimental evidence; and they show conclusively that the

symptoms of "grave jaundice," which I connected with cholesteremia, may be produced by the artificial introduction of cholesterin into the circulation.

As an inevitable result of my observations, confirmed by others and extended by Koloman Müller, I can now confidently repeat the conclusions which I published in 1862.

CONCLUSIONS

I. Cholesterin exists in the bile, the blood, the nervous matter, the crystalline lens and the meconium, but does not exist in the feces under ordinary conditions. The quantity of cholesterin in the blood of the arm is five to eight times more than the ordinary estimate.

II. Cholesterin is formed, in great part if not entirely, in the substance of the nervous matter, where it exists in great quantity and from which it is taken up by the blood and constitutes one of the most important of the effete, or excrementitious products of the body. Its formation is constant and it always exists in the nervous matter and the circulating fluid.

III. Cholesterin is separated from the blood by the liver, appears as a constant element of the bile and is discharged into the alimentary canal. The history of this substance, in the circulating fluid and in the bile, marks it as a product destined to be discharged from the body as an excretion. It preëxists in the blood, subserves no useful purpose in the economy, is separated by and not formed in the liver, and if this separation is interfered with, it accumulates in the system.

IV. The bile has two separate and distinct functions dependent on the presence of two constituents of entirely different characters. It has a function connected with nutrition. This is dependent on the presence of the glycocholate and taurocholate of soda, which do not preëxist in the blood, subserve a useful purpose in the economy and are not discharged from the body, are found in the liver and peculiar to the bile, do not accumulate in the blood when the function of the liver is interfered with, and are, in short, products of secretion. The bile has another function connected with depuration, which is dependent on the presence of cholesterin, which is an excretion. The

flow of bile is remittent, being much increased during the digestive act, but produced during the intervals of digestion for the purpose of separating cholesterin from the blood.

V. The ordinary normal feces do not contain cholesterin but contain stercorin—formerly called “*séroline*” from its being supposed to exist only in the serum of the blood. Stercorin results from a transformation of the cholesterin of the bile during the digestive act.

VI. The change of cholesterin into stercorin does not take place when digestion is arrested or before this process begins; consequently stercorin is not found in the meconium or in the feces of hibernating animals during their torpid condition. These matters contain cholesterin in large abundance, which also sometimes appears in the feces of animals after a prolonged fast. Stercorin is the form in which cholesterin is discharged from the body.

VII. The difference between the two familiar varieties of jaundice, one characterized only by yellowness of the skin and comparatively innocuous, while the other is attended with very grave symptoms and is almost invariably fatal, is dependent upon the obstruction of the bile in one case, and its suppression in the other. In the first instance, the bile is confined in the excretory passages and its coloring matter is absorbed; while in the other, cholesterin is retained in the blood.

VIII. There is a condition of the blood dependent upon the accumulation of cholesterin, which I have called cholesteremia. This occurs only when there is structural change in the liver which incapacitates it from performing its excretory function. It is characterized by symptoms of a grave character referable to the brain and probably is dependent upon the effects of the retained cholesterin on this organ. This occurs with or without jaundice.

IX. Cholesteremia does not occur in every instance of structural disease of the liver. Enough of the liver must be destroyed to prevent the due elimination of cholesterin. In cases in which the organ is but moderately affected, the sound portion is capable of performing the eliminative function of the whole.

X. In cases of simple jaundice, when the feces are decolorized and the bile is entirely shut off from the intestine,

stercorin is not found in the evacuations; but in cases of jaundice with cholesteremia, stercorin may be found, though always very much diminished in quantity, showing that there is an insufficiency in the separation of the cholesterolin from the blood, although its excretion is not entirely suspended. After death, but a small quantity of bile is found in the gall-bladder.

XI

STERCORIN AND CHOLESTEREMIA *

Published in the "New York Medical Journal" for June 5, 1897.

LOOKING far into the future, it seems possible that our successors may fix upon the month of May, 1946, as the true centennial of the American Medical Association, dating the origin of this body from May, 1846, when a convention of representatives of our profession, held in New York, proposed the formation of a National Association, which was formally organized in 1847. If your orator of to-day finds it impossible to do justice to this occasion, how much more difficult will it be to present, in a single address, an adequate picture of a full century of medical progress! The year 1946 will be the centennial of the application of anesthesia to surgery. It will be the third jubilee of the crowning glory of the eighteenth century, the completion of the discovery of vaccination, when the terrible scourge, smallpox, which had been more destructive to human life than war or famine, was virtually subdued. At the Jenner Centenary, held in Berlin in May, 1896, Virchow stated, as an ethnological fact, that "all peoples that had not been reached by vaccination or that had not accepted it had disappeared from the face of the earth, destroyed by smallpox." Will the orator of 1947 be able to point to a triumph of American medicine equal to the application of anesthesia a hundred years before or to the beginning of an era in preventive medicine, like that inaugurated by the immortal Jenner! Looking into the future, it is possible that in fifty years smallpox will have disappeared from the face of the earth, like the peoples it has destroyed. But who can say, in the light of

* Address on Medicine delivered at the semicentennial anniversary of the American Medical Association, in Philadelphia, June 2, 1897.

what has been accomplished within our own recollection, what may not be done within the next half-century! In the single line of preventive medicine, is it not possible that we may be able to secure immunity from tuberculosis, typhus and typhoid fevers, scarlatina, diphtheria and other infectious maladies, and that these diseases may disappear! As it is now, even with a not inconsiderable popular prejudice against vaccination, many successive years have passed in the city of New York without one case of smallpox; and medical knowledge is becoming daily more progressive and more generally accepted by the laity.

It is not too much to say that the convention of May, 1846, marked an era in the history of medical organization in the United States. It had become necessary that the medical profession should be unified and separated from those practising under sectarian designations, particularly as at least one sect was beginning to secure the confidence of men otherwise intelligent, and assumed to practise medicine on a scientific basis. Nearly coincident with the organization of this Association was the discovery to which I have already alluded, that marked a grand epoch in the history of American medicine. On October 17, 1846, practically the first surgical operation was performed under the influence of an anesthetic administered by inhalation. Its semicentennial has recently been impressively celebrated at the Massachusetts General Hospital, in Boston. There are few who remember the horrors of severe surgical operations and the agonies of difficult childbirth before anæsthesia, as there are few remaining who participated in the convention which organized what is now the American Medical Association; but all can realize what surgery would be without artificial insensibility to pain, and what the medical profession would be without a National Association.

The status of medicine forty years ago is quite within my recollection. Medicine is not, never was and never will be an exact science; but it always has been progressive and never more so than at the present time. Fifty years ago perhaps medicine merited the reproach of being the least exact of all sciences; but its progress within the last fifteen years has been so prodigious that it is now in advance of them all. The Abbe illuminating apparatus

made the study of bacteria possible; and this, with the wonderful apochromatic lenses, as it now appears to us, have rendered nearly perfect our technical means of histological and bacteriological research. We no longer differentiate and separate structures by the coarse methods of actual dissection alone; but with the delicate and precise instruments used in cutting thin sections and by staining we have come to an exact knowledge of physiological and pathological histology, which, fifty years ago, seemed unattainable. Without staining fluids, the physiological and pathological histology of the present day would be impossible. Fifty years ago skill in the diagnosis of certain diseases was acquired only by long practice and large experience. With our present methods, properly employed, it is impossible to make an error in the diagnosis of many of the diseases which formerly presented difficulties, such as typhoid fever, tuberculosis, diphtheria, cholera and most of the neoplasms. To say that pathology has been revolutionized within the last ten or fifteen years is not enough—a new pathology has been created, and with it have come an intelligent hygiene, prevention and therapeutics, based upon exact scientific knowledge.

Eleven years ago the great physician whose name I bear and who still lives in the memory of this Association wrote an address which was to have been delivered before the British Medical Association, entitled *Medicine of the Future*. This classic legacy to the profession he so loved and adorned embodied recollections of a half-century of medical observation, with a prophetic view of the possibilities of medicine within the succeeding half-century. It was difficult for this wise physician to restrain his predictions within the bounds of reasonable enthusiasm. The epoch-making discovery of the bacillus tuberculosis, announced by Koch in 1882 and graphically described and illustrated by Dr. Belfield before this Association, at the meeting of 1883, made a most profound impression upon his mind and imagination, which found expression in an elaborate paper on the subject read in January, 1884. His predictions of possibilities in medicine before 1936 are now more than verified. It was predicted that "before the lapse of another half-century there will be another era in organic chemistry, and that light will penetrate dark re-

cesses which histology can not reach." If "light" be taken in its literal sense, is not this more than realized by Röntgen's marvelous discovery, in which a hitherto unknown light is made to penetrate opaque matter and disclose the invisible! In 1886, he wrote: "Moreover, there are present intimations of important discoveries respecting inoculation with attenuated viruses and contagia in order to forestall the development of infectious diseases. Here open up to the imagination the future triumphs of preventive medicine in respect to all classes of disease." Now, little more than ten years later, serum-therapy has taken a permanent place in practice, and we stand on the threshold of a full knowledge of immunity, natural and acquired.

As no human imagination fifty years ago could have pictured the condition of the medicine of to-day, so it to-day seems impossible to imagine its progress in another half-century. Never, since medicine became a science, has medical history been made so fast as now. Between the time of writing and of delivering this address, scientific labor may give birth to a discovery destined to revolutionize some department of medicine, as Pasteur, Koch and their followers have revolutionized therapeutics, and as Lister has created a new surgery.

The reasonable limits of an anniversary address do not permit even an enumeration of the greatest of the advances in the science of medicine since the organization of this Association, much less their discussion. Your orator on surgery will find it impossible adequately to describe the progress of the last half-century in a single address; your orator on state medicine can hardly compass the wonderful advances made even in the single line of prevention of disease; and I certainly can not hope to be more successful.

It is a matter of congratulation that the name of this body was early changed from National to "American Medical Association." We have good reason to be proud of American medicine, and our great representative association may properly claim a distinctive title. When one is able to call up at random the discoveries in gastric digestion, anesthesia in surgery and obstetrics, the successful deligation of the *arteria innominata*, the operation for

vesico-vaginal fistula, ovariectomy and intestinal anastomosis, to say nothing of minor advances in medicine and surgery, can we not claim a distinctive place for American medicine! It is in the United States that advances in the science of medicine find the most ready acceptance and appreciation. The American physician is the most intelligent and judicious therapist; and in the United States are the best and safest surgery and gynecology.

I hope to see, beginning with the second half-century of the American Medical Association, a more complete unity of the profession, through its authority and influence. In the matter of general professional welfare, there seems to me nothing more important than uniformity in medical legislation, and, so far as possible, in educational requirements preliminary to the study of medicine and for license to practise after graduation. Admitting the proposition that the profession is crowded, it is evident that this condition is most serious in the large cities; but overcrowding can not be prevented by legislative enactment, except in so far as unqualified men are excluded. Uniformity of legal qualifications to practise medicine in the different States can best be secured by making every State society actually, as well as nominally, a branch of the American Medical Association, with permanent committees from each State organization together to constitute a central legislative body. The object of this central body should be to secure uniform medical laws in all the States, making any State license valid for all, and a matriculation certificate for one State good for matriculation in all schools represented in the Association of American Medical Colleges. A certain kind of medical instruction must be concentrated in large cities, where clinical material is abundant; and absolute uniformity of curriculum can not exist in all colleges; but certainly the legal requirements for practice, as determined by examination by State boards, can be made practically identical for all the States. While this would not prevent ambitious young men from trying their fortunes in large cities, it would distribute well-qualified physicians more equally in the country at large and tend to raise the standard of qualifications and usefulness of the average country doctor.

It is the prerogative of the presiding officer of this

association to make recommendations, and this is not the province of one appointed simply to give an anniversary discourse. At the jubilee meeting to be held later in the session, it is hoped that the four surviving members of the convention of 1846 will be present. From at least one of these you may expect a more accurate and complete account of the past work of the association and a more intelligent view of its probable future than I am able to give. What I have had the honor to present I well know is entirely inadequate to the occasion, and it has been given merely as an introduction to addresses by others, which will be much more suitable and interesting. The remainder of the time that has been placed at my disposal I shall venture to occupy with a subject which I hope may not prove entirely unworthy of your attention.

STERCORIN AND CHOLESTEREMIA

While the presentation, on this occasion, of researches made and published thirty-five years ago (viewing the question from a physiological standpoint) calls for an explanation and perhaps an apology, none is required if their great importance in relation to the pathology of the liver is considered, especially as cholesteremia is by no means accepted as a distinct pathological condition. Were it not that stercorin has just been rediscovered in Germany by two eminent physiological chemists, who make no mention of its full description in 1862 and have even called it by another name, I probably should not have repeated, and extended my original observations. As it is, however, I feel that I may properly, as an American investigator, make my reclamation before the American Medical Association. Although my paper, published in the "American Journal of the Medical Sciences" in October, 1862, received an "honorable mention" and substantial recognition from the Institute of France and my observations have been verified and extended by French and German investigators, many writers on physiology and pathology, even the most recent, fail to recognize such a substance as stercorin and in treating of cholesterin speak of its function as obscure or unknown.* In "An American

* Foster, "A Text-Book of Physiology," New York and London, 1895, p. 356.

Text-Book of Physiology," Philadelphia, 1896, cholesterin is described as a constant constituent of the bile, very widely distributed in the body and eliminated by the liver-cells from the blood. "That it is an excretion is indicated by the fact that it is eliminated unchanged in the feces." Stercorin is not mentioned. As a matter of fact, cholesterin does not occur in the human feces in health, and its presence in this situation is exceptional.

In Hoppe-Seyler's "Zeitschrift für physiologische Chemie," Strassburg, 1896, is a paper by Bondzynski and Humnicki entitled "The Destination of Cholesterin in the Animal Organism." The authors profess to have discovered a new constituent of the human feces, which they call "koprosterin." This substance is identical with stercorin, fully described in 1862. The reading of this article led me to repeat the original researches of 1862, carrying them out by the methods then employed, at the same time repeating the observations of Bondzynski and Humnicki with the methods and appliances used in their work. It is mainly an account of these new observations that I now give. The chemical manipulations were done by Dr. H. A. Haubold, assistant to the chair of physiology in the Bellevue Hospital Medical College, and J. A. Mandel, assistant in the department of chemistry in the College of the City of New York and to the chair of chemistry in the Bellevue Hospital Medical College. To these two skillful assistants I am indebted for most painstaking and accurate work extending over a period of several months.

The original stercorin, of which specimens obtained in 1862 are in my possession, was extracted from the human feces by the following process: The dried and pulverized feces were extracted with ether. The ethereal extract was passed through animal charcoal and afterward evaporated. The residue was then extracted with boiling alcohol. The alcoholic extract was treated with potassium hydrate solution, at a temperature near the boiling point of water, in order to remove the fats by saponification, which were washed out with water until the filtrate was neutral and perfectly clear. The filter was dried, extracted with ether, and the ethereal extract evaporated to dryness and extracted with boiling alcohol. The stercorin was obtained from the alcoholic extract by repeated crystallization.

This process was exactly repeated in our recent observations, and at the same time stercorin was extracted by the process described by Bondzynski and Humnicki. Normal human feces were obtained to the amount of about fifty pounds. After drying, the feces were divided. Two analyses each were made by Haubold and Mandel, each one extracting stercorin in one portion by the original method, and in the other by the new method. All the extracts obtained were identical in their composition, reactions and the form of crystals. It was fortunate that I had for comparison a fairly large specimen of stercorin extracted in 1862, and a microscopic slide bearing the date of June, 1862, in which the crystals were perfect. The product obtained by my process was a little more abundant and crystallized rather more readily than that obtained by the later method.

- In the process employed by Bondzynski and Humnicki, the dried feces were extracted with ether, using Soxhlet's extraction-apparatus. The fats were saponified with sodium alcoholate. No animal charcoal was used. The substance was purified by repeated crystallizations.
- These variations from the original method are unimportant, except in so far as they expedite the process of extraction. The form of the crystals and the reactions were identical with those which I obtained for stercorin in 1862. Analyses of the products obtained by us, full details of which are given in a paper sent to Hoppe-Seyler's "Zeitschrift," gave, for stercorin, the formula, $C_{27}H_{48}O$, the formula found for cholesterin being $C_{27}H_{46}O$. The change of cholesterin into stercorin is effected by the addition to the former of two atoms of hydrogen. A close comparison of the results of our ultimate analyses with those obtained by Bondzynski and Humnicki shows conclusively that "koprosterin" and stercorin are identical, and that stercorin is not an impure cholesterin, as is held by some eminent investigators, such as Hoppe-Seyler, K. B. Hoffmann and others. Stercorin crystallizes in long, fine needles which radiate from a centre, forming tufts, and which can not be confounded with the characteristic crystals of cholesterin. In a chloroform solution, stercorin gives, with an equal volume of concentrated sulphuric acid, first a yellow color and then a gradual change to orange, red and

finally dark red. Treated in the same way, cholesterin promptly gives a blood-red reaction without these intermediate tints.

The opinion expressed by Hoppe-Seyler, Hoffmann, and indeed many others, that stercorin simply is impure cholesterin, can not have been based upon a practical knowledge of this substance. Stercorin has a well-defined formula ($C_{27}H_{48}O$) which has been calculated and verified by the formation of esters. Its crystals are quite different from crystals of cholesterin and are invariable in form, arrangement and color. It was extracted by methods practically the same as those used in the extraction of cholesterin. In view of these facts, to assume that stercorin is an impure substance one must deny a positive scientific basis to organic chemistry.

In the recent, as well as in the original observations it was clearly shown that cholesterin is changed into stercorin in passing down the intestinal canal. I found that this change involves processes incidental to intestinal digestion. Cholesterin and no stercorin was found in the feces of fasting animals and in the meconium. Bondzynski and Humnicki found an increased proportion of "koprosterin" in human feces after the ingestion of a certain quantity of cholesterin. They also showed that cholesterin united readily with bromine, while "koprosterin" formed no such combination; and, indeed, by the use of bromine, these two substances may be separated when they exist together. They confirmed the empirical formula for their product by the formation of a number of esters.

In 1862 I wrote: "What the discovery of the function of urea has done for diseases which now come under the head of uremia, the discovery of the function of cholesterin may do for the obscure diseases which may hereafter be classed under the head of cholesteremia."

It is now generally admitted that the bile, in addition to its function connected with digestion, contains one or more excrementitious matters. Taking into consideration the various ingredients of the bile, there seems to be but one that can logically be compared to urea. Cholesterin is found in many of the tissues and organs of the body and exists in the blood. Likening it to urea, it becomes

a question whether it is formed in the liver and discharged in the bile or is merely separated from the blood by the liver and excreted. As it is constantly found in notable quantity in the nervous tissue, in the proportion of eight to twelve parts in a thousand, it occurred to me to examine the blood of the internal jugular and compare the proportion of cholesterin with that found in arterial blood. In one experiment on a dog, the blood being taken without using an anesthetic, I found an increase in the jugular over the carotid of nearly sixty per cent. In an etherized animal the increase was only about three and a half per cent. In another dog, not etherized, the increase was about twenty-three per cent. There was also an increase of four to six per cent. in the blood of the femoral vein over arterial blood. In three cases of hemiplegia, the blood from the arm of the sound side contained about the normal proportion of cholesterin, while blood from the affected side contained no cholesterin.

In an experiment on a dog it was found that the arterial blood lost about twenty-three per cent. and the portal blood about four and a half per cent. in passing through the liver, comparing these two kinds of blood with blood taken from the hepatic vein.

These experiments led to an examination of the feces to determine the quantity of cholesterin discharged; but in a number of careful examinations of many different specimens of feces I was unable to find cholesterin. I found, however, what appeared to be a non-saponifiable fatty substance in considerable quantity. Examining this substance daily with the microscope, after five or six days I saw crystals beginning to form, which finally presented the appearances I have already described as characteristic of stercorin. I found the daily discharge of stercorin to be 0.7 gramme, about equal to the estimated quantity of cholesterin discharged into the intestine in the bile in the twenty-four hours. In but one examination of feces of the dog did I find cholesterin, and this was in a fasting animal, a small quantity of cholesterin being found with stercorin. In a specimen of meconium, I found a hundred and sixty parts in a thousand, of cholesterin and no stercorin. In clay-colored feces from a patient with jaundice from obstruction, neither cholesterin nor stercorin was

found. In the feces of the same patient, which were normal in color and obtained fifteen days after the first examination, stercorin was found and no cholesterin. These experimental facts seemed to show that the stercorin of the feces was derived from the cholesterin of the bile, and that the change of cholesterin into stercorin was incidental to the processes of intestinal digestion. In no case was I able to detect in the feces any trace of the biliary salts.

Passing from these observations to the pathological relations of cholesterin, after examining three specimens of normal blood and finding the proportion of cholesterin to be 0.445 to 0.751 of a part in a thousand, examinations were made of the blood of patients with simple jaundice and those with what is called icterus gravis the cases terminating fatally with grave nervous symptoms. In a case of simple jaundice terminating in recovery at the end of about four weeks, the blood contained 0.508 of a part in a thousand, well within the limits for normal blood. In a case of jaundice with cirrhosis terminating fatally with serious nervous disturbance, the blood taken six days before death contained 1.850 part in a thousand, of cholesterin, an immense increase over the normal proportion. In this case, on post-mortem examination, the liver was found contracted, and the gall-bladder was shrunken containing only about seven cubic centimetres of bile.

The question of cholesteremia has been much discussed since 1862, in great part with scant approval or without acceptance. However, Picot,* in 1872, reported a fatal case of "grave jaundice" in which he determined a great increase in the proportion of cholesterin in the blood, 1.804 part in a thousand. Many attempts have been made, also, to produce toxic effects by injecting cholesterin into the blood, but most of them have been unsuccessful on account of mechanical obstruction of the blood-vessels. In 1873, however, Koloman Müller† succeeded by injecting cholesterin rubbed with glycerin and mixed with soap and water. In five experiments on dogs, injecting in each 0.045 gramme of cholesterin, he pro-

* "Journal de l'anatomie," Paris, 1872, tome viii, p. 246 *et seq.*

† Ueber Cholesterämie, "Archiv für experimentelle Pathologie und Pharmakologie," Leipzig, 1873, Bd. i., S. 213 *et seq.*

duced a "complete picture of the symptoms of grave jaundice."

In repeating the original researches of 1862, the observations, as regards analysis of feces, etc., were somewhat extended. With modern apparatus, the manipulations may be freed from many disagreeable features which heretofore, probably, have interfered with this line of investigation. In extracting stercorin, various volatile fatty acids and other substances were removed, the constitution and relations of which are unknown. We studied, in this connection, some of the products of bacterial action, obtaining, by the action of fecal bacteria on proteids, skatol and indol, both substances containing nitrogen. It is well known that phenol and cresol also exist in the feces. These nitrogenous matters are putrefactive products; nothing is known of their physiological or pathological relations, and up to this time stercorin is the only excrementitious matter yet found in the feces, the origin and relations of which are at all understood. Our knowledge, indeed, of the physiological chemistry of the feces is only just begun; and we may look to future investigations for much that will be most important as well as interesting. The same may be said, in a measure, of the bile and of the true pathology of certain functional and structural diseases of the liver. How long shall we continue to speak of biliousness, congestion or torpor of the liver, the classic liver-complaint, "*et id genus omne*," using terms which have no scientific meaning! Undoubtedly there are general disturbances, dependent upon some disorder in the functions of the liver, which occur without jaundice, and this fact has long been recognized. In a case of cirrhosis with considerable constitutional disturbance but no jaundice, the blood was found to contain an excess of cholesterolin, 0.922 of a part in a thousand. In what is termed acholia, there may be grave nervous symptoms without jaundice, and the pathology of such cases is unknown. The biliary salts are not found in the blood, and the symptoms can not be accounted for by disturbances in digestion. It is possible that light will be thrown on their pathology if it is admitted that there is a condition called cholesteremia. As yet this is but speculation; but if the theory of cholesteremia is accepted, a wide field of inquiry is opened in this

direction, and ere long we may speak of "biliousness" and "liver complaint" with some definite ideas of their pathology.

It must be remembered that the liver is by far the largest gland in the body; that it secretes a fluid which is known to have a double function, one connected with digestion and the other with the elimination of cholesterin; that the blood from the digestive tract all passes through this organ, where it undergoes certain changes; that it probably stores up the products of amylolytic digestion in the form of glycogen; that it arrests certain poisons, and that it is the chief organ concerned in the production of urea, which is discharged by the kidneys. It may have other uses in what is now called internal secretion, in addition to that of destruction of blood-corpuscles and the change of hemoglobin into bilirubin. With all these known varied uses of the liver, however, the pathology of hepatic diseases is most obscure. We do not know, even, the cause and mechanism of the formation of gall-stones, which are often composed almost entirely of cholesterin.

The term acholia, as used in pathology, now means very little and conveys no distinct idea of the causes of the nervous symptoms which attend this condition. The term cholemia is generally regarded as almost synonymous with jaundice. If cholesteremia is recognized as a distinct pathological condition, with symptoms due either to the accumulation of cholesterin in the blood, acting as a toxic substance, or to imperfect separation of cholesterin from the nervous tissue, a positive advance will be made in our knowledge of the pathology of many obscure liver disorders.

The quantitative estimation of cholesterin in the blood is not difficult, and it does not require more than four to six or eight grammes of blood. The only tedious manipulations are the drying, saponification and weighing; and these are readily done in a well-appointed laboratory. Some process may be devised which will expedite this extraction. If examinations of the blood were to be made in cases of obscure nervous disturbance, in epilepsy and other disorders of this nature, it is possible that cholesterin may be found to play an important part in their pathology.



FIG. 1.—Cholesterin, 1897.

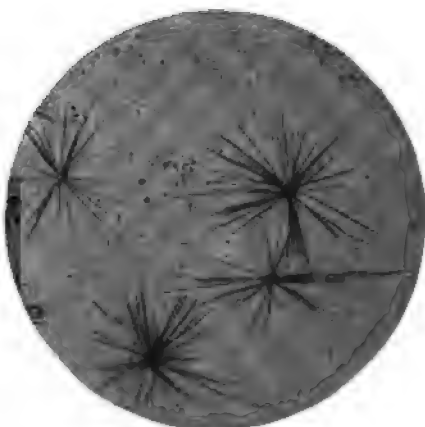


FIG. 2.—Stercorin, Flint, 1897.



FIG. 3.—Stercorin, B. and H., 1897.

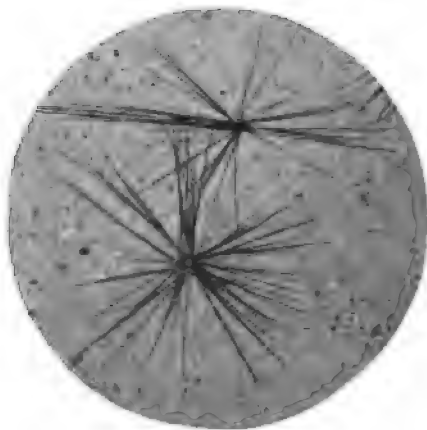


FIG. 4.—Stercorin, Flint, 1862, recrystallized
in 1897.



FIG. 5.—Stercorin, Flint, original slide
of 1862.

Photographs by Prof. E. K. Dunham, M. D. All magnified twenty diameters.

The fact that bromine readily combines with cholesterin, taken in connection with the wide use of the bromides in diseases of the nervous system, is very suggestive. May not the bromides promote the elimination of cholesterin, a substance which is so insoluble and which forms few combinations! These points seem well worthy of the consideration of pathologists and therapeutists. Certainly the physiological and pathological relations of cholesterin offer a wide and perhaps fruitful field for further observation.

With this paper I present photographs of cholesterin, stercorin extracted by the original method, and stercorin extracted by the method of Bondzynski and Humnicki, all in 1897, with a photograph of crystals obtained in 1897 from a specimen of stercorin extracted in 1862.

I have added, for comparison with the recent crystallization from the specimen of 1862, a photograph from a slide marked June, 1862. These crystals, which are from the same specimen of 1862, have been mounted for thirty-five years and are much more abundant and beautiful than those obtained by recrystallization in 1897.

XII

UEBER STERCORIN

(Aus dem physiologischen Laboratorium des Bellevue Hospital Medical College der Stadt New-York. Der Redaction zugegangen am 3. Juni, 1897.)
Published in Hoppe-Seyler's "Zeitschrift für physiologische Chemie," August 28, 1897.

In Folge einer Mittheilung der Herren Bondzynski und Humnicki "Ueber das Schicksal des Cholesterins im thierischen Organismus" in Band XXII, Seite 396-410 dieser Zeitschrift, sehe ich mich veranlasst, aufs Neue auf meine Beobachtungen über Stercorin aufmerksam zu machen.

Die Herren Bondzynski und Humnicki beschreiben unter dem Namen Koprosterin einen neuen Bestandtheil der menschlichen Faeces. Diese Substanz ist identisch mit dem von mir im Jahre 1862 entdeckten und beschriebenen Stercorin. Da die genannten Autoren zur Darstellung des Koprosterins dieselben Processe angewandt und zu denselben Resultaten gelangt sind wie ich, so erscheint es mir angebracht, meine früheren Arbeiten im Vergleich mit den Versuchen von Bondzynski und Humnicki zu besprechen.

Beim Lesen der Arbeit von Bondzynski und Humnicki erscheint es, als ob dieselben glauben, eine neue Substanz im Koprosterin entdeckt zu haben. Es wird des Stercorins und seines Entdeckers keine Erwähnung gethan, obgleich das zuerst von mir beschriebene Stercorin in der deutschen, französischen und englischen Literatur seit 1862 in mehr oder weniger vollständigen Berichten über dessen Eigenschaften und seine Beziehungen zum Organismus erwähnt wird.

Meine Originalmittheilung wurde im Jahre 1862 im "American Journal of the Medical Sciences" in Philadelphia veröffentlicht unter dem Titel "Experimental Researches into a new Excretory Function of the Liver."

Diese Function besteht in der Abgabe von Cholesterin aus dem Blut und seiner Ausscheidung aus dem Körper in der Form von Stercorin. Im Jahre 1868 wurde von G. Baillière in Paris eine Uebersetzung ins Französische veröffentlicht, und im Jahre 1869 erhielt das Werk bei der Bewerbung um den Preis, der Villemains Arbeit über die Contagiosität der Tuberculosis zuerkannt wurde, eine "ehrenvolle Erwähnung" und eine Belohnung von 1500 Francs vom Institut de France. Seit der Zeit sind ausführliche Berichte über Stercorin erschienen in einem meiner Vorträge, veröffentlicht in den "Transactions of the International Medical Congress," Philadelphia 1876, in meinem Werke "Physiology of Man" in 5 Bänden und in meinem Handbuch "Human Physiology," von welchem allein mehr als 20,000 Exemplare verbreitet worden sind; kurze Erwähnungen findet man fast in allen medicinischen Lexika und in Werken über Pathologie, Physiologie und medicinische Chemie. Die Anerkennung, die den gründlichen und exacten Untersuchungen von Herren Bondzynski und Humnicki gezollt werden muss, kann nicht auch auf deren Bekanntschaft mit der Literatur des Gegenstandes ihrer Forschungen ausgedehnt werden. Wäre es anders, so würde ich nicht gezwungen sein, das Recht eines ersten Beobachters auszuüben, nach welchem ich Priorität beanspruche und fordere, dass der Name "Koprosterin" durch "Stercorin" ersetzt werde.

Das ursprüngliche Stercorin, von welchem ich Präparate in meinem Besitz habe, wurde durch folgenden Process aus menschlichem Koth gewonnen.

Die getrockneten und pulverisirten Faeces wurden mit Aether extrahirt. Das ätherische Extract wurde durch Thierkohle entfärbt und dann verdunstet. Der Rückstand wurde darauf mit kochendem Alkohol ausgezogen, das alkoholische Extract mit einer Kalihydratlösung bei einer etwas unter dem Siedepunkt des Wassers liegenden Temperatur verseift, zur Entfernung der Seifen mit Wasser gewaschen, bis das Filtrat neutral und vollkommen klar war. Das Filter wurde dann getrocknet, mit Aether ausgezogen, das ätherische Extract zur Trockne verdampft und mit kochendem Alkohol extrahirt. Das Stercorin wurde aus dem verdunsteten alkoholischen Extract durch wiederholte Krystallisation aus Alkohol gewonnen.

Dieser Process wurde auch bei den neuen Versuchen wiederholt und das erhaltene Produkt ergab bei der Elementar-Analyse die folgenden Resultate:

Nr. I. Substanz 0,2781 gr.; CO₂: 0,8521 gr., H₂O: 0,3064 gr.
 Nr. II. „ 0,2437 „ „ 0,7461 „ „ 0,2701 „

entsprechend

	Nr. I	Nr. 2
Kohlenstoff	83,56%	83,49%
Wasserstoff	12,24%	12,31%

während Bondzynski und Humnicki das Folgende für ihr „Koprosterin“ fanden:

1. Substanz 0,3242 gr., CO₂: 0,9908 gr., H₂O: 0,3595 gr.
 2. „ 0,2954 „ „ 0,9035 „ „ 0,3255 „
 3. „ 0,2684 „ „ 0,8224 „ „ 0,2968 „

entsprechend

	I.	2.	3.
Kohlenstoff	83,24	83,41	83,56
Wasserstoff	12,24	12,24	12,21

Beim Vergleichen dieser beiden Reihen von Resultaten ist es ersichtlich, dass die nach meiner Originalmethode isolirte Substanz mit Koprosterin identisch ist.

Stercorin krystallisirt in langen, feinen Nadeln, die von einem Centrum ausstrahlen und Büschel bilden, und diese Krystalle können gar nicht mit Cholesterinkrystallen verwechselt werden, wie von einigen Forschern, wie Hoppe-Seyler, K. B. Hoffmann u. a., behauptet worden ist.

Die Reactionen des Stercorins sind mit denen des „Koprosterins“ identisch, in Chloroformlösung gibt es nämlich mit einem gleichen Volumen conc. Schwefelsäure zuerst eine gelbe Farbe, welche beim Stehen sich langsam in eine orangerothe und dann in dunkelrothe Farbe umwandelt.

Liebermanns Reaction gibt mit einer Chloroformlösung von Stercorin sofort eine blaue Farbe, die bald von einer grünen gefolgt wird.

In dem von Bondzynski und Humnicki angewandten Process wurden die getrockneten Faeces mittelst Soxhlets Extractionsapparat mit Aether extrahirt. Die Fette wurden mit Natriumalkoholat verseift. Thierkohle wurde nicht angewendet, sondern die Substanz wurde durch wiederholte Krystallisation gereinigt. Diese Abweichungen

von meiner ursprünglichen Methode sind unwesentlich, sie beschleunigen nur den Extractionsprocess. Das nach dieser Methode erhaltene Produkt ist sowohl bezüglich der Krystallform wie auch der chemischen Eigenschaften mit Stercorin identisch. Die Feststellung dieser That-sachen ist genügend und es ist überflüssig, der äusserst sorgsamten Arbeit der Herren Bondzynski und Humnicki Weiteres hinzuzufügen.

In meinen neuen, ebenso wie in den früheren ursprünglichen Beobachtungen, habe ich klar nachgewiesen, dass Cholesterin beim Durchgang durch den Darmkanal in Stercorin umgewandelt wird. Ich fand, dass diese Veränderung auf den Processen der Darmverdauung beruht. Cholesterin und kein Stercorin wurde in dem Koth von fastenden Thieren und im Meconium gefunden. Bondzynski und Humnicki fanden nach Einnahme einer bestimmten Menge Cholesterin eine vermehrte Menge Koprosterin in den menschlichen Faeces.

Diese Forscher berechneten die Formel $C_{27}H_{48}O$ für "Koprosterin" und $C_{27}H_{46}O$ als Formel für Cholesterin. Hieraus ergibt sich, dass die Veränderung des Cholesterins in "Koprosterin" auf dem Eintritt von zwei Atomen Wasserstoff beruht. Sie zeigten auch, dass das "Koprosterin" keine Verbindungen mit Brom bildet, wie dies beim Cholesterin der Fall ist. Durch Brom können auch diese beiden Substanzen getrennt werden, wenn sie zusammen vorkommen.

Die Beobachtungen von Bondzynski und Humnicki waren rein chemischer Natur. In meiner Originalarbeit untersuchte ich zunächst die physiologischen Eigenschaften und Beziehungen der Galle in ihrer Bedeutung sowohl für die Verdauung und Resorption als auch für die Excretion. Ich studirte dann das Cholesterin, wie es in gewissen Organen, Geweben und Flüssigkeiten des Körpers gefunden wird. Ich zeigte, dass die Menge des Cholesterins im Blute vermehrt wird bei dem Durchgang des letzteren durch das Gehirn und verhältnissmässig verringert wird beim Durchgang durch die Leber, und wies nach, dass Cholesterin, wenn es ein Ausscheidungsprodukt ist, wahrscheinlich zum grössten Theil das Resultat von Umsetzungen im Nervengewebe ist.

Dann zeigte ich die Verwandlung des Cholesterins im

Dünndarm und entdeckte Stercorin in den Faeces in einer Quantität, die der Menge des in der Galle ausgeschiedenen Cholesterins fast gleich kam.

Eine Entschuldigung dieses Prioritätsanspruchs auf die Entdeckung des Stercorins als eines Bestandtheils der Faeces und dieses Protestes gegen den Namen "Koprosterin" mag aus der hohen Wichtigkeit der Beziehung dieser Substanz zum Cholesterin und aus der grossen Bedeutung des von mir als Cholesteraemie bezeichneten Krankheitszustandes hergeleitet werden.

Ich bin weit davon entfernt, irgend einen Vorwurf gegen die Herren Bondzynski und Humnicki zu beabsichtigen, ich bin ihnen sogar zu Dank verpflichtet, da ihre von den meinen unabhängigen Beobachtungen wahrscheinlich veranlassen werden, dass die Existenz des Stercorins und der Cholesteraemietheorie die allgemeine Anerkennung findet, auf welche ich, mit wenig oder gar keiner Ermuthigung, 35 Jahre gewartet habe.

Zu gleicher Zeit nehme ich Veranlassung, meinen Assistenten, den Herren H. A. Haubold und J. A. Mandel, meinen Dank auszusprechen für ihre gewissenhaften und anerkennenswerthen Arbeiten bei der Wiederholung der ursprünglichen Darstellung des Stercorins.

XIII

ON THE ORGANIC NITROGENOUS PRINCIPLES OF THE BODY WITH A NEW METHOD FOR THEIR ESTIMATION IN THE BLOOD

PART I

Published in the "American Journal of the Medical Sciences"
for October, 1863.

COMPOSITION AND PROPERTIES OF THE ORGANIC NITROGENOUS PRINCIPLES OF THE BODY.—The physiological investigator of the present day is greatly dependent upon chemistry for methods of investigating the functions of the body; so much so, indeed, that these departments can not be separated from each other; and it is to physiological chemistry he must look for the solution of questions of the highest importance which yet remain unanswered. Of the various questions which thus remain to be answered by the chemist, that of the quantity, composition, condition of existence and changes of the organic nitrogenous principles is the most important; for these apparently are the constituents of the body endowed with vital properties; they regulate the changes which take place in the other principles, and the various modifications which they undergo in the body constitute the mysterious "life," the comprehension of which has not yet been granted to the student of Nature. Though chemistry has enabled the physiologist to make but little if any progress toward the solution of the great question of vitality, it has helped him to comprehend certain of the phenomena of living bodies; and by long searching he has found out some of the laws which regulate their phenomena. The results of the physiological labors of centuries have only confirmed an axiom which must be recognized by every one who hopes to make any advance in this science.

The laws which regulate animated Nature are irrevoc-

cably fixed; as distinct from those which govern inanimate objects as life is from death. They must be sought for by a patient study of the phenomena of life, until the chain of evidence is complete. The mind must seek to comprehend, not to create.

Much ineffectual labor has resulted from a lack of comprehension of this idea. While physiology was comparatively new as a science, many endeavored to establish laws for the regulation of the economy instead of adding to actual knowledge of phenomena; and others, ignorant of the fact that what is true of inanimate matter can not be applied to the living body, endeavored to explain everything by physical or chemical laws. To this latter may be attributed the want of application of chemistry to physiology until within the last few years; though, in all ages, when learning has been cultivated, chemistry has been a favorite study. Those who took such pride in the discovery of elements and the establishment of physical laws could not bring themselves to admit, and can not at the present day admit that the body is anything but a collection of elements regulated by the laws with which they are familiar; while those who saw these laws so often violated in living bodies were disposed to reject entirely chemical and physical explanations of physiological phenomena. To make use of chemistry, from which physiology had so much to expect, it was necessary to create a new method of study which would have reference to organic substances and to substances not necessarily chemical elements but formed from these elements, which are now called proximate principles. It will be seen at once how important are these principles with reference to their condition and behavior in the living body, and how necessary it is to study them from this point of view and not simply as inorganic or inanimate compounds.

There is thus a manifest difference between proximate principles and chemical elements. The former have certain properties in the living body which are different from any known in the inorganic world. They may have properties peculiar to animal substances, like albumin or myosin, which are endowed in living bodies with the vital properties of continual destruction and reparation; or the substance may be inorganic, as water or chloride of sodium, but actu-

ally entering into the composition of organized tissues and participating in the peculiar changes which they undergo. The latter are indivisible substances, possessing no power of self-regeneration, forming definite compounds by union with other elements of the same class, by which union the properties of the component parts are radically changed. Chemical elements can be studied, and have been studied for years, without reference to organized or living structures; though these are formed necessarily of such elements, and as such have been found to possess certain definite properties. When the chemist, in investigating organic bodies, studies only the ultimate elements of which they are composed, he learns nothing more of the properties of these elements, for they are identical with those he extracts from inorganic substances. He gives simply the results of decomposition of the body; but what the physiologist wishes to know is the function of the systems and organs and the elements which compose the tissues of the body. The ultimate composition of organic bodies is manifestly of little importance compared with a knowledge of their physiological properties; unless, indeed, this should explain their function, a hope of the chemist which is rarely realized. Thus the body can not advantageously be studied from a purely chemical point of view; and the changes which take place, even in its inorganic constituents, can not be explained by formulas which indicate simply the addition or subtraction of certain elements. Within a few years a great advance has been made in physiological chemistry by a modification of the method of study of organic matters. The most rational investigators of the present day treat them as compound substances, which can not be decomposed without destroying their peculiar properties. But a still further advance is necessary: they must be considered, not merely as proximate principles, which can be separated from the body by means which do not interfere with their chemical composition, but as principles capable of performing their functions only when united together, as they certainly are in Nature. For example, what has been considered as albumin, that is, dried albumin, is incapable of performing its function if it is not united with water, chloride of sodium and other inorganic substances which are always found in connection with it; and though

it is important to know its ultimate composition and its behavior on the application of heat, in the presence of acids, etc., etc., these phenomena are artificial and useful only as tests. The true line of inquiry lies in a study of its behavior in the body and the investigation of natural, rather than artificial phenomena. Instead of attempting to isolate it completely, it should rather be studied in its union with the other principles by which it is enabled to perform its functions; and when it is separated from the animal fluids in order to ascertain its proportional quantity, it should be separated with those other substances which are united with it in the living body and without which it can perform no vital functions. It will be seen that some of these substances, as water, actually enter into the composition of the organic principles and can not be separated without alteration and decomposition.

These preliminary remarks explain why I consider it of the greatest importance to study, first of all, the condition under which organic substances exist in the body, especially as this question is almost ignored by physiologists. To correspond with the ideas I shall present upon this question, a new method of estimating the quantities of these substances is necessary, as the ordinary analyses are the work of chemists who have not appreciated their condition of existence. In discussing this question I shall review to some extent the opinions and analyses of chemists, which are accepted at the present time.

ULTIMATE COMPOSITION OF ORGANIC NITROGENOUS SUBSTANCES.—According to the present views, every tissue of the body and all the fluids, with the exception of the excrementitious fluids, contain a characteristic element, which is found in no other situation and which gives certain properties connected with nutrition, which may be called vital. These tissues and organized fluids contain usually but one characteristic organic principle. With the exceptions of the blood and milk, there is but one such element to each tissue or fluid. The blood, however, which furnishes the material for the formation of all these substances, contains several organic principles; viz., fibrin, albumin, and globulin; and the milk contains, in addition to casein, a trace of albumin. Although it is probable that all the tissues and organized fluids (excre-

mentitious fluids excepted) contain principles of this kind, which are characteristic and present shades of difference for each one, some have not yet been separated sufficiently for purposes of study; and according to Robin and Verdeil, only seventeen can be regarded as well established.*

LIST OF ORGANIC NITROGENOUS SUBSTANCES

Name.	Where found.
Fibrin.....	Blood, chyle, lymph.
Albumin.....	Blood, chyle, lymph, serum, milk.
Albuminose.....	Chyme, blood.
Casein.....	Milk.
Mucosine.....	Mucus.
Pancreatine.....	Pancreatic juice.
Globuline.....	Blood-globules.
Musculine.....	Muscles.
Osteine.....	Bone.
Cartilageine.....	Cartilage.
Elasticine.....	Elastic tissue.
Keratine.....	Nails, hair, epidermis.
Crystalline.....	Crystalline lens.
Hematine.....	Coloring matter of the blood.
† Biliverdine.....	" " " bile.
Urosacine.....	" " " urine.
Melanine.....	" " " pigment.

Of the seventeen principles above enumerated, only three have been studied with any degree of accuracy; namely, fibrin, albumin and casein. The proportion of these principles in the fluids in which they have been found has been carefully estimated; and in addition much pains has been bestowed upon their ultimate analysis. Albumin has given the name to nearly all these substances, from similarity, as far as known, of composition, and the others, called albuminoids, have been simply indicated in the situations above enumerated, no attempt having been made, with one or two unimportant exceptions, to estimate their quantity or to ascertain their ultimate composition. In fine, the blood and the milk are about the only fluids of the body which have been subjected to critical analysis for organic substances, and hardly anything has been done with the solids. I do not propose in this article to take up the chemistry of the milk; and throwing out this fluid, I am reduced in my examination of analyses to the organic prin-

* "Traité de chimie anatomique," Paris, 1853.

† These are simply coloring matters and are put by Robin and Verdeil in this class as they contain nitrogen.

ciples of the blood, which have justly claimed the most careful investigation at the hands of physiological chemists.

In the latter part of the last century Bertholet demonstrated the existence of nitrogen in organic bodies. Before his time chemists had little idea of their composition. It was known that they were very unstable, and the discovery of the above-named ingredient offered a supposed explanation of this fact; viz., that its presence engendered a number of "attractions" which did not operate in bodies of a less complicated composition. This discovery was a great advance in the chemical knowledge of organic substances of this class; and the researches of investigators since that time have so far established it, that they are known generally under the name of nitrogenous, or azotized principles. The organic matters were afterward closely studied by Dumas, especially those existing in the blood; and, indeed, the mode of analysis of this fluid for its organic constituents, employed by Dumas forty years ago, is the one adopted, with but slight modifications, by chemists of the present day. He ascertained, in the first place, the quantity of water which could be driven off from the blood, and attributed it all to the serum, considering the fibrin and albumin as held in solution by this water and the globules as possessing no fluid of their own. By appropriate means, which will be considered hereafter, he separated the fibrin, albumin and globules, evaporated them to dryness and estimated them in this condition. The ultimate composition of these principles was not then definitely ascertained; and no theory of the mode of union of their elements or their formation was proposed. A few years later (1837), in connection with Liebig, Dumas proposed a division of chemical science into inorganic, or mineral, and organic. According to the theory proposed, all inorganic bodies were composed of two elements directly combined, forming what they called binary compounds, which again united with other compounds formed in the same way. Thus, potassium and oxygen united to form potash (KO), which, in its turn, can unite with another binary compound, as nitric acid (NO_5), to form nitrate of potash (KO.NO_5); the elements first uniting together to form pairs, which in their turn unite with each other. In inorganic chemistry the union of elements proceeds in this simple manner to

form the most complex substances; an element can unite only with an element, a binary compound, with a binary compound, and so on. Organic, particularly vegetable substances, on the contrary, were theoretically reduced to the compounds of a radicle which, though itself a compound, behaved toward elementary substances in the same way as a simple inorganic element. In other words, the behavior of these so-called organic radicles in their union with elementary substances would lead one to suppose them to be elements themselves; it is only chemical analysis which shows them to be compound. For example, cyanogen will unite with hydrogen to form hydrocyanic acid (HCy), as chlorine will unite with hydrogen forming hydrochloric acid (HCl). The latter is an inorganic or mineral acid, and the chlorine, which is the radicle, is of necessity an elementary substance; but cyanogen, the radicle of the organic acid, though it unites with the element hydrogen in the same way as the chlorine, behaving like an elementary substance, is found by chemical analysis to be a compound of carbon and nitrogen (CN). It is in reality a radicle, but compound; and a compound radicle is a thing unknown in inorganic chemistry. The example just given shows a marked difference in the behavior of inorganic and organic substances, as the radicle CN, or cyanogen, actually exists and conducts itself, not as a compound, but as an elementary substance; and if all organic compounds could be shown to be formed of compound radicles, this would constitute a true distinction between inorganic and organic combinations. But this is not the case; though some chemists have theoretically reduced alcohol, ether, acetic acid, and in fact all organic vegetable compounds, to a union of elements with compound radicles, these radicles, unlike cyanogen, are hypothetical. It is said, for example, that the radicle ethyl (C_2H_5) unites with oxygen to form the oxide of ethyl (C_2H_5)₂O), which is ether; but ethyl never exists in nature and can not be manufactured. The same is true of the radicles, methyl, acetyl, benzyl, ammonium, etc. The hypothetical character of these radicles is universally acknowledged,* and the theory

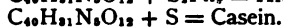
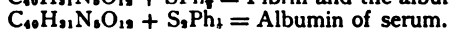
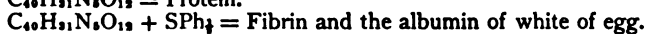
* For a summary of the history of these so-called organic radicles the reader is referred to a lecture by M. Auguste Cahours, published by the "Société chimique de Paris," 1860, p. 51.

of compound organic radicles, although it may serve to explain the composition of certain classes of organic bodies, is not universally received by chemists of the present day; it is rather a mathematical analysis than an actual investigation of real substances; for with the exception of one or two, all these radicles are hypothetical. This wholesale assumption of imaginary substances violates, in toto, the axiom enunciated at the beginning of this article. Instead of studying the behavior of organic bodies, phenomena are imagined and facts distorted to correspond with laws which are known to regulate the behavior of inorganic substances. But it is beyond the scope of this paper to treat of these purely chemical questions; and the reason the theory of organic radicles has been discussed at all is that it was followed the next year (1838) by the theory of Mulder, by which he attempted to explain the constitution of the albuminoids. He supposed all organic nitrogenous substances in the body to be formed by the union of certain elements with a radicle, protein, giving to them the name of protein compounds. This hypothesis was adopted by Liebig, Dumas and Simon and is now accepted by many physiologists.

PROTEIN.—As before remarked, the only albuminoids that have been carefully studied are fibrin, albumin and casein. In addition to a great similarity in the general properties of these substances, ultimate analysis has shown a remarkable likeness in chemical composition. It is not to be wondered at, then, that an attempt should be made to reduce all the compounds of this class to a series derived from a common radicle, following upon the theory of organic vegetable radicles. This was done by Mulder; who, treating albumin, fibrin or casein with alcohol and ether to remove fats and with hydrochloric acid to remove inorganic salts, dissolved these matters, thus purified, in a solution of potash and precipitated by acetic acid a substance said to possess always the same characters, which he called the radicle of the albuminoids, and which, by union with a certain quantity of sulphur and phosphorus, was capable of forming fibrin, albumin or casein. This, which is merely an extension of the theory of compound organic radicles into animal chemistry, has a more plausible basis than in the case of vegetable organic compounds. The supposed

radicle, protein, was obtained and analyzed by Mulder; and if it could be definitely established to be the same for the various substances from which it is extracted, and if these substances could be shown to consist always of this radicle with a definite proportion of sulphur or sulphur and phosphorus, the theory would be sustained so far as possible with present means of investigation. It is true it would be sustained only by analysis; but synthesis has not yet been applied to animal chemistry. But the protein theory is not susceptible of analytical demonstration. The composition of protein itself is not definitely settled; and a review of the methods of ultimate organic analysis will show that the varied results obtained by chemists do not depend on a want of accurate means of analysis but upon the indefinite characters of the compounds themselves. Take, for example, the analyses of Mulder * showing the composition of the protein groups, and compare them with the results obtained by other chemists!

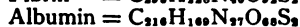
Mulder gives the following formulas for the protein group:



These analyses by Mulder have been confirmed by Schröder and Von Laer.†

Regnault gives as the constitution of protein $C_{36}H_{23}N_4O_{10}$; ‡ Sheerer, $C_{48}H_{72}N_{12}O_{14}$; * Liebig, $C_{48}H_{36}N_6O_{42}$; and Dumas, $C_{48}H_{25}N_6O_{17}$.||

The composition of fibrin, albumin and casein, given by Dalton and credited to Liebig, is as follows: ^A



* Robin and Verdeil, "Chimie anatomique," tome i., p. 652.

† "Animal Chemistry with reference to the Physiology and Pathology of Man." By Dr. J. Franz Simon. Philadelphia, 1846.

‡ "Cours élémentaire de chimie," etc. Par M. V. Regnault. Paris, 1853, tome iv., p. 114.

* Milne Edwards, "Leçons sur la physiologie," etc. Paris, 1857, tome i., p. 151.

|| Robin and Verdeil, *op. cit.*, tome i., p. 651.

^A Dalton, "Treatise on Human Physiology." Second edition. Philadelphia, 1861, p. 80; and Robin and Verdeil, *op. cit.*, tome iii., p. 147.

Denis, in a paper presented to the Academy of Sciences at Paris in 1839, advanced the view that fibrin and albumin are identical in composition; and this view was sustained by Liebig in a note to the Academy in 1841.*

With this diversity of opinion among chemists, based on actual analyses, it is difficult to come to any conclusion other than the following:

There is no evidence that fibrin, albumin and casein are formed by the union of a definite proportion of phosphorus and sulphur with a common radicle.

In addition it is certain, if any weight is to be attached to ultimate analyses, that the properties of these substances do not depend entirely on their chemical composition. According to the analyses of Mulder, even, it is seen that two substances as dissimilar as it is possible for substances of this class to be, namely, albumin of the white of egg and fibrin, have the same ultimate composition. The ultimate composition, then, does not seem to be important as regards the general properties of the compound.

Notwithstanding all the labor that has been bestowed upon the ultimate analysis of the substances under consideration, the question of their composition does not seem to be one of any great importance. The difficulties of such analyses and the contradictory results in the hands of skilful chemists show that a knowledge of the ultimate composition of organic nitrogenous substances is of little value as a means of distinguishing them from each other; and such analyses throw no light whatever on their function in the economy. A careful review of the facts which have been accumulated on this subject leads to the conclusion that these bodies are of indefinite chemical composition. In the first place they are not crystallizable; second, they may be made to assume different forms and properties by the action of imponderable agents, as in coagulation by heat or galvanism, without losing or gaining any elements; third, they are in a continual state of change, in nutrition during life, without losing their properties, and will continue to absorb oxygen and exhale carbonic acid for some time after removal from the body,† and shortly

* Robin and Verdeil, *op. cit.*, tome iii., p. 282.

† G. Liebig has shown that the muscles of the frog will continue to absorb oxygen and exhale carbonic acid after they have been separated from the body,

after these properties have disappeared, undergo the changes of putrefaction; finally, there is no great difference between them in chemical composition, and almost all the analyses made by chemists of equal skill present great variations. Is there not, then, every support for the assertion that their chemical composition is indefinite! Either this assertion is correct or the methods of analysis employed are inaccurate. As so much depends upon this point, I venture to give a rapid sketch of the method of analysis most commonly employed by chemists.

It is first ascertained, by a very simple process, that a given substance, as albumin, is composed of certain elements, as carbon, hydrogen, oxygen, nitrogen, sulphur and phosphorus. This being determined, it is deprived of moisture; the fat is removed by ether and alcohol; and the earthy salts, as far as possible, by dilute hydrochloric acid. A carefully weighed quantity is then decomposed, and the proportions of these elements are determined in the following way:

A tube of the hardest glass, half an inch in diameter, sixteen to eighteen inches long, and closed in a flame at one end, is used for the decomposition, which is effected by combustion. The oxidation is effected by means of the black oxide of copper, which is prepared for the purpose perfectly pure, carefully powdered and completely freed from moisture. The tube is first filled for two or three inches with pure oxide of copper. The organic matter is now to be carefully powdered, incorporated with oxide of copper (it is best to employ five to eight grains of organic matter for the analysis), taking care that none is lost, and the mixture is introduced into the tube. The tube is now to be filled to within an inch of its extremity with pure oxide of copper.

In this part of the manipulation, care should be taken to remove all moisture, as this would affect the quantity of hydrogen obtained from the combustion. This may be done by attaching the tube, after it has been filled, to one opening of a small airpump, such as is used for this purpose, the other being fitted to a bent tube filled with pumice stone and sulphuric acid. By placing the combustion tube

so long as they retain their contractility. Lehmann, "Physiological Chemistry," Philadelphia edition, vol. ii., p. 474.

in a long dish filled with warm water and exhausting the air a few times, all the moisture may be removed.

As the tube is to be subjected to intense heat, it should be wound with a narrow ribbon of sheet brass, which will prevent its bending when it becomes softened. There is now to be attached to the open end, by a smaller tube fitted perfectly with a cork, a light tubular apparatus filled with small fragments of chloride of calcium, the tube and its contents having been previously weighed, and connected with this is a series of bulbs, called Liebig's potash bulbs, partly filled with a solution of caustic potash, which is likewise to be carefully weighed. The heat may now be applied to the combustion tube, which may be done in a long glass furnace made for the purpose, or by surrounding it, well supported in a long iron trough, with hot coals. The heat is applied gradually, beginning at the nearer end of the combustion tube. The organic substance is thus completely decomposed; and if it is composed of carbon, hydrogen and oxygen, like sugar, the analysis will be complete, this combustion giving the carbon and hydrogen, the oxygen being obtained by difference. As it is, all the hydrogen is converted into watery vapor, which is absorbed by the chloride of calcium, and the carbon, converted into carbonic acid, is absorbed by the potash. The weight of these products is ascertained by taking the increase of weight of the calcium tube and the potash bulbs, and the quantities of carbon and hydrogen are deduced therefrom.

There remain now the nitrogen and sulphur. The same tube, with a little modification, may be used for carbon, hydrogen and nitrogen; but it is better to estimate the nitrogen in another apparatus. For this purpose a combustion tube is used similar to the one just described, placing at the closed end a few grains of bicarbonate of soda; then the oxide of copper as before; next the mixture of oxide of copper and the organic matter; next another layer of pure oxide of copper, and last of all a layer of pure copper reduced by hydrogen. The extremity is then connected with one opening of the airpump, and to the other is adapted a tube which opens under a receiver containing mercury with a solution of potash floating on the top. The air is then exhausted as completely as possible and the combustion tube is connected with the receiver by opening both

stopcocks of the airpump. It is necessary now to drive out all the air from the apparatus, to collect the pure nitrogen in a gaseous form. For this purpose heat is applied to the farther extremity of the tube, which decomposes the bicarbonate and carbonic acid gas is evolved. It can be seen that all the air is driven off, by the complete absorption of the gas evolved by the potash in the receiver, showing that pure carbonic acid is coming over. Another receiver filled with mercury and a solution of potash is then substituted, the heat from the bicarbonate is withdrawn and applied gradually from the anterior portion of the tube as before. Combustion of the organic matter takes place, which results in watery vapor, carbonic acid, which is absorbed by the potash in the receiver, and nitrogen, which passes over and is collected in a gaseous form. Some of the nitrogen is oxidized by this combustion, but as it passes over the hot metallic copper in the nearer extremity of the tube, the oxygen is retained and the nitrogen passes over pure. After the combustion of the organic matter is complete, heat is again applied to the bicarbonate of soda so as to drive off what nitrogen remains in the tube, by the evolution of carbonic acid. It remains now to remove the receiver, substitute water for the mercury, measure the volume of the gas, taking the temperature carefully and bringing the level of the water in the tube to that of the surrounding liquid, and thence deduce its weight, which gives the proportion of nitrogen.

The sulphur and phosphorus, if there is any, exist in very small quantity. They may be estimated in the albuminoids without any great difficulty, by causing them to unite with soda, as sulphuric or phosphoric acid, and then precipitating with the chloride of barium for the sulphur, and by a process a little more complicated, but not less exact, for the phosphorus, which it is not necessary to describe here.

In this manner are obtained the weights, in a given portion of albumin, of all its ingredients but the oxygen; viz., carbon, hydrogen, nitrogen and sulphur. Subtracting the sum of the weights of these substances from the whole weight, gives the oxygen; and reducing to 100 parts gives the ultimate composition.

I have given the process rather fully, to show how, with

certain precautions, in the hands of one skilled in chemical manipulations, it may be made as accurate as any operation in inorganic chemistry. With a balance that will turn with less than $\frac{1}{1000}$ of a gramme, and with care to avoid moisture, etc., in the apparatus, the result should be always the same, if the substance analyzed had always the same composition.

The next step is to establish the formula in equivalents. If the substance used is an acid or a base which combines with any substance of known combining equivalent, this could be easily done, by getting the weight of a combining atom by experiment, calculating the proportions of its ingredients to this weight, and dividing the quantity of each element thus obtained by its combining equivalent. But in the case of the albuminoids, which are neutral, this can not be done. A formula is calculated for them which expresses the elements in the simplest manner so as to give no fractions, generally giving an even number for the atoms of carbon. Thus Liebig gives as the formula for fibrin, $C_{298}H_{228}N_{40}O_{92}S_{12}$.*

This review of the mode of ultimate analysis of organic nitrogenous bodies makes it evident to one conversant with chemical manipulations, that the contradictory results obtained by different chemists are not due to imperfections in the analytical process; indeed, the process is acknowledged by chemists generally to be as accurate as that for the determination of the composition of inorganic substances. The only way, then, to explain the contradictory results obtained by different chemists of equal skill and reputation, is to assume that the chemical composition of the principles is indefinite. While enough has been said, perhaps, to convince the reader of this, it follows that important results are to be expected rather from a study of the condition and behavior of these substances in the economy than their decomposition into elements. When they have been extracted from the body, they are by no means in the condition under which they normally exist. This being

* It is hoped that the reader of this article will remember that it was written in 1863, when physiological chemistry was in its infancy. I have preferred to publish the part relating to organic chemistry as it first appeared, correcting only a few of the formulas, rather than attempt to adapt it to modern ideas or omit it entirely.

the case, it is for the physiological chemist to give their quantity, properties, etc., so far as he can, in the condition in which they really exist in life; the physiologist then takes them and studies the phenomena in which they are concerned. Here comes the important question: What is the condition of existence of the organic nitrogenous elements in the body? On the answer to this question depends the mode of proximate analysis of the organized fluids of the body, especially the blood, which is all important to the physiologist.

CONDITION OF EXISTENCE OF ORGANIC NITROGENOUS SUBSTANCES IN THE BODY.—In the ordinary proximate analysis of the blood, by which is meant an analysis giving the proportions of proximate principles without any reference to their ultimate composition, the albumin and fibrin are put down in very small proportions. Fibrin is recognized by its spontaneous coagulability, and albumin, by its coagulability by heat and nitric acid; and it is evident that fibrin may be extracted from the blood coagulated on rods, and the albumin of the serum solidified by heat or nitric acid, in quantities which are much greater than those given in analyses. The physician finds it difficult to reconcile to his ideas of albumin and fibrin of the blood, the proportions of sixty to sixty-five parts per thousand for albumin, and two and a half for fibrin. The reason why the estimates fall so far below our ideas is that chemists never have estimated the fibrin and albumin as they are separated from the fluids by coagulation, which changes only their form and not their weight, but after separating them in this way, have subjected them to perfect desiccation. They have given, therefore, not the weight of the principles as they exist, not the fibrin and albumin in a condition to nourish the body, but the desiccated substance, altered, and its properties destroyed by this process. Physiologists assume that fibrin and albumin are in solution in the water of the blood, and that their natural condition, in a state of purity, is that of a dry powder. In this case it is extremely difficult to reduce these substances to their natural condition. When coagulated, which, according to this view, is a precipitation, a large quantity of water persistently remains, which it is very difficult to get rid of; and when got rid of, the dry substance must be weighed quickly and with

many precautions to avoid absorption of moisture. Other matters are also found combined with coagulated organic matters. All the salts found in the blood are united with them as well as water; and in the proximate analyses, these salts are generally not separated from the organic substance before it is weighed. This view, which is almost universally held by physiologists, is the one which has guided all the analyses of the organized fluids. Of the original works to which I have access, that of Robin and Verdeil, on "Anatomical Chemistry,"* is the only one in which I find any dissent from the prevailing doctrine. They regard the organic elements of the fluids as naturally liquid and not in solution; those of the semisolids as naturally semisolid; and of the solids as solid. The contrary view seems to me radically and entirely wrong; and all analyses of the organized fluids, made under the idea that organic substances are in solution, fail to give anything like a correct notion of the properties of these substances. The analyses of the blood which are embodied in the latter part of this paper are the only ones, so far as I know, which have been attempted with reference to the real condition, as it seems to me, of the organic constituents. They have been made on the following principle:

The water which is contained in coagulated organic substances and which may be driven off by dry heat is not part of the water which held the organic matter in solution, but an actual constituent of the substance, as much as carbon, hydrogen or nitrogen, and is indispensable to the properties by which it is recognized as an organic principle.

It has already been shown that ultimate analysis does not give an idea of the distinctive characters of different organic matters. This depends upon certain characters which are found in all principles of this class, and further, upon certain properties which serve to distinguish them one from another; and when deprived of their water of composition by desiccation, neither in their general properties nor in chemical composition are there any means of recognizing them, unless it is by their indefinite chemical composition and the impossibility of making them assume a definite or crystalline form.

* *Op. cit.*, tome iii., p. 121.

First, in regard to their general properties! They all undergo a change peculiar to themselves, called putrefaction. This property, which is the one perhaps most distinctive of organic matters, disappears when they are deprived, even partially, of water; a fact that is well known and of which there is a familiar example in the preservation of meats. Again, when an organic substance is in a state of putrefaction, it is capable of inducing the same change in other elements of this class, by what is called catalysis, or acting as a ferment. As water is necessary to putrefaction, it consequently is necessary to the development of this property. Principles of this class also undergo a change peculiar to themselves in cooking, which is characterized by the development of volatile empyreumatic substances. Water is necessary to this change, for if exposed to heat after water has been driven off, as has already been seen in the study of the method of ultimate analysis, they are resolved into their elements without undergoing any such change. They also are capable of regaining their water of composition after desiccation, possessing to an eminent degree what is called the property of hygrometricity, by which they are returned to the condition they assumed when first coagulated. This coagulability is also a peculiar property, entirely different from precipitation from a solution. They can not be redissolved in the liquid from which they are separated by coagulation. For example, all of them, including albumin, are insoluble in alcohol; but if albumin is coagulated by alcohol and afterward freed from it, it can not be redissolved by pure water or by the liquid from which it was separated. When once coagulated they have undergone a change and can not be redissolved except by means which change them still more. When they have been coagulated and dried, reduced to what is called a condition of purity, they can not be redissolved and detected by their property of coagulation; for they are changed and consequently are not in their natural condition.

Fibrin may be described as an organic constituent of the blood, which possesses the property of coagulating when removed from the body, giving this property to the whole mass of blood, which separates after a time into clot and serum. Albumin may be described as a principle

of the same class, existing in the serum, which is coagulated by heat or nitric acid. These are naturally fluid, but coagulate, in the one instance spontaneously, and in the other, by the means just mentioned. It can not be said that they are principles composed of so many atoms of carbon, nitrogen, etc., because their composition is indefinite. As regards the proportion of these principles contained in the blood, one can say only that after they have been separated from this fluid and after all their water has been driven off, there have been found $2\frac{1}{2}$ parts of fibrin, and 60 or 70 of albumin per 1,000. This conveys little idea of the real quantity, but only the quantity of anhydrous matter contained in these substances, not the quantity of coagulating fibrin and albumin found in the blood. Analyses giving the quantities of these substances as nearly as possible in their natural condition have never been made; although they would seem the only ones that could convey any definite idea of what is most important to know. I have attempted to supply this deficiency, to a certain extent, in Part II., on the Analysis of the Blood.

I have enumerated nearly all the properties by which one can recognize organic nitrogenous substances, separated from the living organism, as a class; namely, putrefaction, the property of becoming ferments, changes in coction, desiccation, hygrometricity and coagulation; and all of these depend on the presence of water. Should it not, then, be almost conclusive from these facts that water is a necessary and very important element in their constitution! It is true that it is separated with great facility, and that its union with the other constituents is not very powerful; but this is no argument against the fact of its being in a condition of actual union. There are many substances in the inorganic world which have a union no more powerful than that of water in organic matters. Take the single example of the bicarbonate of soda. The second equivalent of carbonic acid is driven off by gentle heat and even by exposure to the air at the ordinary temperature, leaving the salt in the condition of a carbonate.

There is another circumstance in connection with the mode of union of water with other ingredients to form an organic body which serves to distinguish it from mere solution. When a solid substance, as a salt, is in solution

in any liquid, it requires a certain quantity of the liquid to dissolve a certain quantity of the solid; but beyond this the liquid may be increased indefinitely, the solid having the same relation of solution to the whole mass. On the contrary, when one chemical compound, as nitric acid, unites with another, as with soda, one equivalent of the one combines with one equivalent of the other, and if more of either one is added, it does not enter into combination. I regard the organic substances found in the liquids of the body as naturally liquid and mixed with the other liquids; the water which enters into their composition, as represented by the water which they contain when separated from the other liquids by coagulation; and this quantity of water, though not absolutely definite, is as definite in its proportion as are the other ingredients. It is restricted within definite limits; and although, when liquid, like many other liquids it may be mixed with an indefinite quantity of water, when separated by coagulation, water will always be found in about the same proportion.

There is another point of view, by far the most important physiologically, from which to study this question of the natural condition of the organic constituents of the liquids. Do they conduct themselves in the processes of nutrition like the inorganic substances, which are undoubtedly held in solution, or like substances naturally liquid?

This question seems to me very easily answered. The processes of nutrition of the organic constituents of the body consist in a change of the liquid organic substances, principally the albumin and fibrin, into those which are semisolid and solid, like myosin, ossein, etc. In the process of these changes, water is of course absolutely necessary, and is deposited with the other constituents of the organic matters. It, as well as the carbon, hydrogen and nitrogen, is necessary to the constitution of the myosin and ossein and is involved in all the changes incident to nutrition.

Having special reference to the blood and the organic substances which it contains, the relations between this fluid and the tissues constitute one of the most important and interesting of physiological inquiries. In the organic constituents of the solids and semisolids of the body reside, undoubtedly, the vital properties which lead them to regen-

erate themselves at the expense of the circulating fluid; and in the tissues and organs, as well as in the blood, the organic matters are always united with inorganic salts, as well as with water. Of these salts, some, in connection with organic matter, go in great measure to make up the tissues, as the phosphate of lime in the bones; while others seem by their presence to regulate the nutritive processes, like the chloride of sodium, which is more abundant in the blood than in the tissues. Organic nitrogenous matters, whether fluid, semisolid or solid, never exist alone, but always in combination with inorganic substances. It is impossible, indeed, in extracting the organic substances from the body, to free them entirely from inorganic salts; and the fibrin and albumin of the blood I have found to contain all of the salts which exist in that fluid. The blood contains all of the elements, both organic and inorganic, which are necessary for the regeneration of the tissues. The inorganic elements are deposited unchanged, and in the organic elements alone resides that property of mutual convertibility which forms myosin, chondrin, ossein, etc., out of albumin and fibrin. In this process of change there is a deposition of the salts, which can not take place by itself but must be involved in the deposition of organic matter. This process is not to be explained by the laws of chemical attraction or represented by a change in chemical formulas. It takes place only in organic living bodies; and the more we attempt to elucidate it by investigations of a purely chemical nature, the farther we remove ourselves from a comprehension of the essence of nutrition. We must learn to look on processes like this as physiological and not chemical; and as we never have constructed, and perhaps never shall construct, a single organic nutritive substance out of its elements, or changed one into another, so we shall ever fail to comprehend the phenomena of change and the mystery of their construction in the body, if we persist in endeavoring to adapt these phenomena to the laws which regulate the composition and changes of inorganic substances. When we study the composition of these substances, we should take them as we find them, and not try to reduce them to a condition approximating that of minerals. The absence of useful results following the labors in this direction of so many chemists

should be a warning to us to leave the beaten track. When we study their properties, we have already seen that it is necessary to take them as they are, combined with water, or these properties are lost. When we come finally to study their functions in the economy, we find that they not only contain water, but inorganic substances, which are indispensable to the great function of nutrition, and which can not be separated from the organic. We must in this study recognize the following important facts:

First. Organic nitrogenous substances are the only elements of the body in which reside the properties of destruction and regeneration during life. Fats, sugars, and inorganic salts operate with them, and by virtue of this property.

Second. They are of indefinite chemical composition; and no great physiological importance is to be attached to ultimate analyses. They are unstable, in a state of continual change during life and soon alter after death or after removal from the body.

Third. They assume the consistence of the tissue or fluid in which they exist. They are solid in the solids, like bone; semisolid in the semisolids, like muscle; liquid in the liquids, like the blood. They are not dissolved in water, but water is an ingredient, and its quantity determines their consistence.

Fourth. In the body they never exist alone, but are always combined with inorganic substances, which accompany them in the changes which they undergo in the processes of nutrition and disassimilation.

Fifth. As all the proximate analyses of the organized fluids, particularly the blood, have been made with the idea that the organic ingredients were solids in solution in water, these quantitative analyses give, not the proportions of fibrin or albumin, but dried fibrin and albumin, the original substance subjected to a process which drives off its most important constituent and which alters its properties. Such analyses, as representing real quantities, are erroneous.

PART II

ANALYSES OF THE BLOOD WITH REFERENCE TO ITS ORGANIC CONSTITUENTS.—From the review just given of the organic constituents of the body and the intimate relation seen to exist between the tissues and the blood, it is evident that an analysis of the nutritive fluid, especially with reference to its organic constituents, is of great interest and importance. This has long been recognized; and in late years a great part of the labors of investigators in physiological chemistry have been devoted to this subject. It is not my purpose here to consider any but the organic principles of the blood. The constitution of this fluid, in its entire physiological and pathological relations, is too extended a theme to be considered in this place. The fact that the blood contains certain excrementitious substances shows that this fluid is connected with the waste as well as the repair of the system. The pathological importance of this has been settled experimentally by the discovery of the accumulation of excrementitious matters in the circulating fluid, giving rise to certain pathological conditions; as for example, urea, producing a condition of the system known under the name of uremia; and more lately, the discovery of the character of cholesterin as an excretion and its accumulation in the blood, under certain conditions of the liver, constituting cholesteremia.* These are only two examples where diseased conditions of the system have been clearly shown to depend upon the accumulation of a specific excrementitious substance in the blood; but the work in this direction is but begun; and I venture to predict that more light will be thrown on pathology by the discovery of new toxins in the blood, dependent on defective excretion, than by any other line of experimental inquiry.

The proximate analyses of the blood up to this time have been made under the supposition that the organic matters, fibrin and albumin, are solid matters in solution; but according to the views advanced in Part I.; namely, that their real condition is one of fluidity, and that when

* See an article on a "New Excretory Function of the Liver," by the author, published in the number of this Journal for October, 1862.

deprived of water they lose one of their most important constituents, this mode of analysis is inadmissible. The actual quantities of fibrin and albumin can no more be represented by the residue of evaporation than by the residue of calcination, which latter would leave only inorganic matter. Before giving, however, the processes by which I have attempted to estimate the quantities of undried fibrin, albumin and globules in the circulating fluid, I shall give a rapid review of the methods of proximate analysis which are now generally employed.

Berzelius, followed soon after by Marcet, made the first extended quantitative analyses of the blood. He analyzed the serum of human blood and indicated certain quantities of albumin, lactate of soda, muriate of soda, etc. He put the quantity of dried albumin at 80 parts per 1,000, which is about the proportion given in the analyses of chemists of the present day. His researches were published in 1808 and were followed by the analyses of Marcet, in 1811, which gave nearly the same results. In 1823 Prevost and Dumas published their researches on the composition of the blood, with a full account of their process. This process, with slight modifications, is the one employed generally at the present time. The following are the principal steps in the analysis: The fibrin is separated from a weighed quantity of blood by whipping with a bundle of broom-corn, carefully collected, dried and weighed. Another specimen of blood is set aside to coagulate, and after it has fully separated into clot and serum, the clot is dried and weighed; the proportion of fibrin ascertained from the first specimen is subtracted, which gives the quantity of dried globules. The serum is then evaporated to dryness, the residue extracted thoroughly with boiling water, ether and hot alcohol, to remove inorganic salts and fats and afterward weighed, which gives the proportion of albumin. The fats are easily extracted with ether; and the inorganic constituents are estimated after incineration, by a process which it is not necessary to describe. This process has been followed, with unimportant modifications, by a number of chemists, who have done little more, in regard to the albumin and fibrin, than confirm the observations of Prevost and Dumas. Among these may be mentioned Andral and Gavarret, Becquerel and Rodier, Sheerer, and Simon.

Among these observers, perhaps, the process adopted by Becquerel and Rodier is one as generally accepted by physiologists as any, and I shall therefore translate from their work, entitled "*Traité de chimie pathologique*," so much of it as refers to the estimation of the fibrin, albumin and globules:

"FIRST SERIES OF OPERATIONS.—This is designed to furnish: First, the density of the blood and that of the serum; second, the weight of fibrin and globules and of the solid matter of the serum taken as a whole. These processes are founded on the same principle which served as the basis of the process devised long since by M. Dumas. We suppose that all the water contained in the blood forms part of the serum and should be attributed to it. Still, in admitting this principle, we have not always applied it in the same manner.

"The following is our mode of operation:

"We practise upon the person whose blood we wish to analyze, a bleeding of about 375 grammes. The blood which first flows from the vein is received in a glass vessel, graduated and capable of holding about 125 cubic centimetres of this liquid. We collect it and whip it with a bundle of broomcorn. We thus obtain the fibrin, which we must wash, desiccate and weigh.

"The blood, thus defibrinated, is then put aside to serve for other operations.

"The blood which flows from the vein, after these 125 cubic centimetres, is collected with care in a vessel of the capacity of 250 to 300 cubic centimetres and left to itself. This blood coagulates, and once the coagulation effected, we separate carefully the serum, which we put aside in a vessel; as to the clot, after having taken note of its physical characters, we may set it aside.

"Let us see now what we do; first, with the defibrinated blood; second, with the serum.

"A. The defibrinated blood is first weighed at a definite temperature in a glass specific-gravity bottle.* We compare then the weight which we obtain in this operation with the weight of the same volume of distilled water; and we thus have, by a very simple calculation which it is useless to reproduce here, the exact weight of the 125 cubic centimetres of blood which we whipped to separate the fibrin, and consequently the weight of this same fibrin contained in 1,000 grammes of blood. Once this operation effected, we take a definite quantity of defibrinated blood, which we weigh, which we desiccate, which we afterward weigh anew, and we thus have the weight of the quantity of water which it contains. Let us take, for example, in order to make ourselves better understood, arbitrary numbers which we shall make use of also to deduce the weight of the globules: 100 grammes of defibrinated blood, liquid,

* All our specific-gravities were taken at a temperature of 12° (53.6° Fahr.) and compared exactly with distilled water at the same temperature.

gives 20 parts of solid material and 80 parts of water. Then 20 parts, thus dried, are calcinated to give us the inorganic matters; we shall return to this.

"B. The serum.—After having determined the specific gravity of the serum, we take a given quantity of this liquid which we weigh, which we desiccate, which we afterward weigh anew; the difference of these two weights gives that of the water; as, for example, 100 grammes of liquid serum having given 10 grammes of solid matter and 90 grammes of water. These operations terminated, we possess the figures necessary to deduce the weight of the globules and that of the solid matters of the serum contained in 100 grammes of defibrinated blood. Indeed, as all the water of the defibrinated blood should be attributed to the serum, we must make the following proportion:

$$80 : x :: 90 : 10 \text{ or } x = \frac{80 \times 10}{90} = 8.8 \text{ gr.}$$

"This proportion 8.8 represents the sum of the solid matters of the serum contained in 100 grammes of defibrinated blood, and subtracting that from 20, the weight of this blood desiccated, we have 11.2 which represents the weight of the globules, and in calculating the whole to 1,000, we have 1,000 grammes of blood, containing:

Water.....	800 grammes.
Globules.....	112 "
Solid matters of the serum.....	88 "

"The weight of the fibrin has been given by the first operation and should be added. Its weight is so small in proportion to 1,000 grammes of blood, that we may neglect a little correction which we should have to make for the weight of the fibrin in addition to the 1,000 grammes of defibrinated blood.

"Such is the first series of operations; for the second we shall make use of the dried serum, and for the third, of the defibrinated blood calcinated.

"SECOND SERIES OF OPERATIONS.—These operations are designed to give the weight of the extractive matters and that of the fatty matters. The following is our mode of operation:

"The serum, having been dried with precaution in an 'étuve,' and pulverized with the greatest care, is treated repeatedly with boiling water until this water has completely freed it from everything which it can dissolve. These last are, on the one hand, extractive matters, such as osmazome, the coloring matter of serum, etc., etc., and on the other hand, the salts which are in solution in the serum and are in a free state.

"The serum, thus extracted with water, is dried again and weighed, the difference from the weight obtained by the first weighing indicates that of the matters we have mentioned and which the water has removed. The product of the second desiccation is then treated with boiling alcohol at 90°, until it is completely extracted. The insoluble residue is pure albumin, of which we may take the weight after having dried it. As to the boiling alcohol, it holds in solution all the fatty matters, which can be separated by em-

ploying the process indicated by M. F. Boudet, and of which we think it unnecessary to give a description. It gives the serolin, cholesterin and saponifiable fats." *

The above quotation is a fair representation of the mode of analysis most commonly made use of at the present day. It differs, however, very little from that indicated by Dumas. There are certain objections to this process, aside from those which have reference to the estimation of fibrin and albumin, which have long engaged more or less the attention of physiological chemists and are acknowledged to be well founded. It will be observed that all the water is attributed to the plasma, while the globules are estimated dry. This is manifestly faulty, as the most cursory microscopic examination of the blood-globules is sufficient to show that they have a consistence dependent upon the presence of a certain quantity of water; and though it may be convenient to estimate these bodies dry, such an estimate gives no idea of their real proportion. This was appreciated as long ago as 1828, by Denis, who attempted to give the proportions of moist globules by a process which had avowedly little accuracy and which he afterward abandoned for the original process of Dumas.† In 1844 Figuier published an analysis of the blood which gives an estimate of the moist globules by a process that I have employed in the analyses which follow, and which seems to me to give sufficiently accurate results, although Denis does not consider it superior to his own. This process was accepted by Dumas with some modifications which are described by him in the "Annales de chimie et de physique" for 1846, p. 452. The process of Figuier depends on the property which certain saline substances have, mixed with the blood, of retaining the globules on a filter. The modification by Dumas is intended to avoid a difficulty which sometimes occurs from alteration and liquefaction of the globules, by which some pass through a filter and are lost. It consists in passing a continuous current of air through the filtering fluid, which prevents this change. In the analyses I have made I have not found it necessary to adopt this precaution.

* Becquerel and Rodier, *op. cit.*, p. 21.

† "Mémoire sur le sang." Par P. S. Denis (de Commercy). Paris, 1859, p. 51.

The following is the process described by Figuier, translated from the "*Annales de chimie et de physique*." * It was not used by him to determine the proportion of moist globules; the globules are merely separated from the blood, dried and estimated in this condition like the other organic matters.

"The blood furnished by a venesection is whipped on its discharge from the vein according to the process of M. Dumas. The fibrin separates and adheres to the little broomcorns. The liquid is passed through a fine cloth to separate that portion of the fibrin which does not adhere to the broom. This fibrin is then washed in a current of water, then dried in a water-bath, and weighed, after having been treated, if desired, with ether to remove a little fatty matter.

"In taking the total weight of the blood which has given this quantity of fibrin, we shall have the proportion of the fibrin to the other elements of blood.

"We then take 80 or 90 grammes only of the defibrinated blood which we treat with about twice its volume of a solution of sulphate of soda marking sixteen to eighteen degrees in the *aërometer* of Baumé, and this is thrown on a half-filter weighed in advance, and previously moistened with the saline solution; with these precautions the serum filters quite rapidly with a yellowish color.

"We understand that, to remove from the globules that remain on the filter, the solution of sulphate of soda with which they are impregnated, we can not simply wash the filter, for that would dissolve a portion of the globules and the fluid would pass red like the blood. But a property peculiar to the globules allows us, happily, to surmount this difficulty. When they are heated to 90° Cent., as Berzelius has already seen, the globules are coagulated entire, and the entire mass becomes concrete without yielding to the water any of the organic matter. We have only, then, to place the filter in a capsule containing boiling water, repeating this process two or three times. The sulphate of soda is dissolved and the water takes almost nothing from the globules, for the fluid is almost colorless and does not contain any organic matter appreciable by tannin or corrosive sublimate.

"To separate the albumin from the filtered serum it suffices to carry it to the point of ebullition in a capsule. The albumin coagulates; it is collected in a little net of fine cloth; it is washed and weighed, after having been dried, by the water bath. Finally, to determine the quantity of water contained in the blood, we take twenty or twenty-five grammes which we evaporate to dryness in a water bath. The weight of the residue indicates the proportions of water and solid elements.

* "Sur une méthode nouvelle pour l'analyse de sang, et sur le constitution chimique des globules sanguins." Par M. L. Figuier.—"*Ann. de chim. et de phys.*," 1844, 3^{me} série, tome xi., p. 506.

"The soluble salts of the serum are represented by the difference of the weight of the blood employed and the sum of the albumin, water, fibrin and globules determined directly."

The above is a very simple and accurate process for determining the globules and organic constituents of the blood, but according to the view already indicated, it is open to the same objection as the other, as it gives the quantity of these ingredients dried, and not as they really exist.

Schmidt, of Dorpat, recognizing the necessity of a proper estimate of the moist globules, endeavored to establish a certain proportion of water to be constantly attributed to them; so that by adding this quantity to the estimate of the dry globules by Prevost and Dumas and others, their results could be made use of. He endeavored to do this by comparative microscopic measurements of the moist and dry globules, and he arrived at the conclusion that the dry globules multiplied by four would give the quantity of moist globules. Though this process was adopted by Lehmann as the most accurate, it is evident that it can not possibly be exact; especially if the proportion of water in the globules is not always the same, as is stated by Zimmermann.

Zimmermann attempted to give the proportion of water in the globules by estimating the quantity of chlorides in the blood, assuming, with Berzelius, that all the chlorides are contained in the serum and there exist none in the corpuscles. He estimated first the proportion of the chlorides in the serum, then the quantity of chlorides in a given quantity of blood, whence he deduced the proportion of serum in the blood; then subtracting the water contained in the serum from the water contained in the entire blood, he obtained the proportion of water in the globules. As it is by no means certain that the blood-globules contain none of the chlorides, this process can not be accepted.

Other methods of a very complicated character have been proposed by Vierordt, Le Canu and Lehmann, which it is not necessary to describe, as they present no advantages over the foregoing.

The most recent process that has been proposed originated with Denis and was published by him in

1859.* His manipulations to get rid of the interstitial serum of the globules are complicated, difficult and of questionable efficacy. He arrives, by this process, at very nearly the results I have obtained by the process of Figuier, which, from its simplicity, is much to be preferred.

From this brief review of the processes for the analysis of the blood, especially with reference to the fibrin, albumin and globules, it is seen that no analysis has ever been made, or even attempted, which would give the real quantities of fibrin and albumin; in all of them the dry residue, and not the substance itself, is given. In the estimation of the globules, however, this desiccating process is so evidently faulty that efforts have been made to estimate them in their moist state, or as they really exist. As yet there is no one process for arriving at this end that is generally accepted by physiological chemists. From my own observations in regard to all the constituents under consideration, it seems impossible to make an analysis which will be perfectly accurate; but absolute accuracy is not indispensable. One can get near enough to the truth for all practical purposes; and as the comparison of different analyses made in the same way gives them much of their value, it is best to fix upon that process for estimation of the moist globules which is simplest and which seems to give the most reliable results. It is manifestly better to get an approximate idea of the fibrin, albumin and globules of the blood in the condition in which they really exist than to take the quantity of dry residue, which gives no idea whatsoever.

Having in view, then, the condition of existence and functions of the organic constituents of the blood, it is only an estimate of these principles in a moist state that can give any clear idea of their proportions.

ANALYTICAL PROCESS.—In the process which I shall describe, I have endeavored to simplify manipulations so far as is consistent with reasonable accuracy, deeming it important to put such investigations within the reach of every one rather than to complicate the process by precautions which are designed to avoid errors so slight that they

* Denis, *op. cit.*

may practically be disregarded. Dumas has shown that the composition of the blood is not precisely the same at the beginning and the end of a bleeding; and he recommends, therefore, that the blood be drawn in equal quantities in four vessels, defibrinating the specimens in the second and third, and allowing those in the first and fourth to separate into clot and serum. By comparing the results of the separate analyses, a correction may be made. I have not found it necessary to use more than two specimens of two to four ounces each; and with this quantity such a precaution is not necessary.

It is very important to cover the vessels which contain the blood and to weigh them as soon as possible; for the specimens lose weight very rapidly by evaporation, as has been shown by Becquerel and Rodier,* which would seriously interfere with the quantitative analysis.

The blood to be analyzed is taken from the arm and received into two carefully weighed vessels. The quantity in each vessel may be two to four ounces. One of the specimens is whipped with a small bundle of broomcorn, previously moistened and weighed, so as to collect the fibrin; and after the fibrin is completely coagulated, the whole is carefully weighed, deducting the weights of the vessel and broomcorn, which gives the weight of the specimen of blood used. The other specimen is set aside to coagulate.

The first specimen is to be used for the estimation of fibrin and globules; the second is set aside to coagulate and is used to estimate the albumin.

The first specimen of blood is now passed through a fine sieve to collect any fibrin that may not have become attached to the wisp; the fibrin is stripped from the wisp and washed under a stream of water. This may be done very rapidly by causing the water to flow through a small

* In experiments by Becquerel and Rodier with reference to the loss of weight by evaporation, the following results were obtained. The blood was drawn into a porcelain vessel about two and a half inches in diameter:

	Weight of blood on being drawn from the vein.	Weight of blood 2 hours after.	Weight of blood 24 hours after.
1st Exp. . . .	13.242 grammes	13.070 grammes	11.510 grammes
2d Exp. . . .	14.905 "	14.727 "	12.977 "
3d Exp. . . .	22.453 "	22.308 "	20.337 "

—"Chimie pathologique," p. 31.

strainer, so as to break it up into a number of little streams, and kneading the fibrin in the fingers, doing this over a sieve so as to catch any particles that may become detached. In this way it may be freed from the globules in five or ten minutes. The fibrin thus washed is then freed from adherent moisture by bibulous paper and is weighed as soon as possible. The following simple formula gives the proportion per 1,000 parts of blood:

Weight of blood used : Weight of fibrin : : 1,000 : Fibrin per 1,000.

The next step is to estimate the globules. For this purpose a portion of the defibrinated blood, which is carefully weighed, is mixed with twice its volume of a saturated solution of sulphate of soda and thrown on a filter which has been carefully weighed, moistened with distilled water, and just before receiving the mixture of blood and the sulphate of soda is moistened with the saline solution. The fluid which passes through should be about the color of the serum; and if a few globules pass at first the fluid should be poured back until it is clear. The funnel is then covered and the fluid allowed to separate, the blood-globules being retained on the filter. The filter and funnel are then plunged several times in a vessel of boiling water, by which all the sulphate of soda which remains is washed out and the blood-globules are coagulated without changing their weight. The funnel should be covered again and the water allowed to drip from the filter, after which it is weighed, deducting the weight of the moist filter previously obtained, which gives the weight of the globules. The proportion of globules to 1,000 parts of blood is obtained by the following formula:

Defibrinated blood used : Globules : : Defibrinated : Globules per
blood per 1,000 1,000.

The next step is to estimate the quantity of albumin in the serum and thence its proportion in the blood. For this purpose I first ascertain the quantity of serum in 1,000 parts of blood, which is done by subtracting the sum of the fibrin and globules per 1,000 from 1,000. Having done this and waited ten or twelve hours for specimen No. 2 to separate completely into clot and serum, I take a small quantity of the serum, about half an ounce, carefully weigh it, and add suddenly twice its volume of

absolute alcohol. The albumin is thus thrown down in a grumous mass, and the whole is thrown on a filter previously moistened with alcohol and weighed. The funnel is immediately covered, and the fluid separates from the albumin very rapidly. I ascertain that no fluid albumin passes through the filter by testing the fluid with nitric acid. After the filter has ceased to drip, it is weighed, and the weight of albumin ascertained by deducting the weight of the filter. The proportion of albumin to 1,000 parts of blood is obtained by the following formula:

Serum used : Albumin : : Serum per 1,000 : Albumin per 1,000.

The above process is very simple and easy of application; and if the directions are carefully followed, it will give quite uniform results. I have repeatedly satisfied myself of this fact by subjecting two specimens of the same blood to the same process, which was followed by almost identical, and in some instances, identical results. For example, in an examination of human blood, two equal quantities (34.20 grammes) of defibrinated blood were analyzed for globules; one specimen gave 16.40 grammes of globules, and the other 16.43 grammes. This part of the process would seem more open to the charge of inaccuracy than any; yet the difference in the results of the two analyses is so slight that it may be disregarded.

In washing the fibrin I was at first led to use a saline solution instead of pure water; but as the mass evidently gained weight treated in this way, I afterward employed simple water. Of two specimens of fibrin from the same blood, one, which was washed with a solution of common salt, spec. grav. 1.010, gave 10.28 parts per 1,000, and the other, which was washed with water, gave but 8.82 parts, a diminution of about 14 per cent.

I tried most of the methods for coagulating the albumin before fixing upon the one by absolute alcohol. The object was to get it as nearly as possible in its natural condition, simply changing its form from fluid to semisolid, without adding anything which would decompose it or unite with it; and absolute alcohol seemed better than heat, nitric acid, the galvanic current or any of the agents by which it is coagulated. It is necessary to add about twice the volume of alcohol, and to do this suddenly; when the fluid

which separates by filtration will be found to contain not a trace of albumin. Repeated trials of different specimens of the same serum, producing generally identical results, led me to fix upon this as the best method.

It is easy to see, after a few trials, why this method of estimation of these organic matters has not been employed by chemists. The difficulty is to fix the standard of moisture; for the specimens, even when on the balance, lose weight by evaporation every moment. This, of course, is opposed to the ideas of accuracy which are necessarily ingrafted into the character of every good analytical chemist. One who is accustomed to weigh for hours, perhaps, to avoid a possible error of the thousandth of a gramme, could hardly consent to accept a weight which is changing every moment. Complete desiccation is the only absolutely definite standard; and in all these organic animal analyses, the substance is weighed and exposed to heat over and over again, until it ceases to lose weight. Although such accuracy is indispensable in some processes in physiological chemistry, here it is not only unnecessary but impossible. It is part of the nature of these substances to change every moment; and when they are reduced to such a condition that they will no longer change, they have lost all their characteristics as organic principles. What is most desirable is an approximate physiological idea of their real quantity; and this is better than the most accurate estimate of their dry residue.

By the process just described, I have arrived at the following results in the few quantitative analyses of the blood for organic principles I have made. The variations in these constituents in different states of the human system and in different animals are interesting and important; but this demands time and a long series of investigations. In the few observations here presented, it has been my object to show the advantages of the analytical process employed, so that it can be applied by others, and to give merely an analysis of the healthy human blood; and the various experiments have been made rather to be able to fix upon a definite process than with a view to comparative results. Attention has been directed only to fibrin, albumin and globules, for reasons which have already been fully given. The number of analyses of human blood is not large, for it is not easy to obtain healthy specimens; and with the

improved notions of therapeutics, it is difficult, also, to obtain specimens of blood from patients. The specimens of human blood were taken from the arm. The blood of the ox was taken in the slaughter house, the vessels of the neck being divided after the animal had been knocked on the head.

EXAMINATION I.—HUMAN BLOOD, MALE.—This specimen of blood is assumed to be perfectly normal. The subject is twenty-seven years of age, male, perfectly healthy and has never suffered from disease. The weight is one hundred and seventy pounds. The blood was taken from the arm at 1 P. M. The last meal had been taken at 8 A. M.

The following is the result of analysis of the blood:

Fibrin.....	8.82	parts per 1,000.
Albumin.....	329.82	" "
Globules.....	495.59	" "

EXAMINATION II. — HUMAN BLOOD, MALE. — This specimen was taken from a man, thirty-seven years of age, calker by trade, weight two hundred pounds, but rather corpulent than muscular. He had slight constitutional syphilis, and had been taking the iodide of potassium, gr. x three times a day, for about three weeks. He was bled from the arm about two hours after dinner.

The following is the result of analysis of the blood:

Fibrin.....	7.44	parts per 1,000.
Albumin.....	277.55	" "
Globules.....	480.44	" "

EXAMINATION III.—HUMAN BLOOD, FEMALE.—This specimen was taken from a female, twenty-seven years of age, weight one hundred and sixty pounds, dark complexion, and perfectly healthy, with the exception of a slight plethoric tendency, as indicated by occasional epistaxis which had troubled her for a few days. She menstruated regularly, the last time about two weeks ago. She took lunch about 11 A. M. and was bled at 2 P. M. The blood coagulated rapidly, and in twelve hours the clot presented the "buffed and cupped" appearance. A portion of the defibrinated blood which was not used in the analysis presented a remarkable example of gravitation of the globules and separation from the serum. It stood in a graduated glass, and the upper half, by actual measurement, con-

sisted of pure serum.* Two days after the venesection the woman still enjoyed perfect health.

The following is the result of analysis of the blood:

Fibrin.....	16.81	parts per 1,000.
Albumin.....	311.18	" "
Globules.....	484.51	" "

EXAMINATION IV.—HUMAN BLOOD, FEMALE.—This specimen was taken from a woman, twenty-eight years of age of somewhat anemic aspect. She had been taking an ounce of sulphate of magnesia every second day for two weeks. The medicine usually operated three or four times. She was bled at 2 P. M., having eaten nothing since 8 A. M.

The following is the result of analysis of the blood:

Fibrin.....	11.34	parts per 1,000.
Albumin.....	219.47	" "
Globules.....	382.95	" "

EXAMINATION V.—BLOOD OF THE OX.—This specimen was taken from a small ox, the throat being cut after he had been knocked in the head.

The following is the result of the analysis:

Fibrin.....	14.52	parts per 1,000.
Albumin.....	195.24	" "
Globules.....	623.36	" "

EXAMINATION VI.—BLOOD OF THE OX.—The animal from which this specimen was taken was rather larger and more vigorous than the one which furnished the blood for Examination V.

The following is the result of the analysis:

Fibrin.....	16.27	parts per 1,000.
Albumin.....	200.85	" "
Globules.....	568.61	" "

Of the four observations on the human subject, but one, Examination I., can be taken as a fair example of normal blood. This analysis shows that the moist globules constitute about one-half of the entire mass of blood; an

* This tendency of the globules to gravitate in defibrinated blood was noticed by Poiseuille, and is mentioned by Bernard who advances the view that one of the important functions of fibrin is to keep the globules in uniform suspension. (Bernard, "Liquides de l'organisme," tome i., p. 465.) This is by no means invariable. I have seen specimens of blood in which there was no gravitation of the globules. Such a complete separation as was presented in this specimen of blood is very remarkable.

estimate which does not differ much from the results obtained by others who have endeavored to solve this question. Denis gives the proportion of globules in a person "30 years of age, strong constitution, sanguine temperament," 489.52 parts per 1,000.* Schmidt estimates the moist globules at 513 per 1,000 for the male and 396 for the female.† Lehmann estimates them at 496 per 1,000.‡

Albumin constitutes by far the greatest part of the other organic matters and equals nearly one-third of the entire weight of blood. As this is undoubtedly the element which nourishes the organic parts of the tissues, which form the greatest part of the body, its preponderance is not surprising. The fibrin, even by this mode of analysis, is seen to exist in small quantity, sufficient, however, to firmly coagulate the whole mass of blood. One is surprised in washing a large clot to see how little fibrin is necessary to thus entangle all the globules. The salts were found to exist in the fibrin, albumin and globules, which were all tested for chlorides, carbonates, phosphates and sulphates.

Taking Becquerel and Rodier as authority for the proportion of fatty, inorganic and extractive matters, the following table represents the composition of the blood in a healthy adult male (the author):

COMPOSITION OF THE BLOOD *		
	Globules.....	495.59
Plasma.	Water.....	155.42
	Fibrin.....	8.82
	Albumin.....	329.82
	Fats, inorganic salts, and extractives (B. & R.).	10.35
		<u>1,000.00</u>

Physiologists have not yet sufficient data to arrive at any definite conclusions in regard to variations in the organic constituents of the blood as regards sex, conditions

* Denis, "Mémoire sur le sang," Paris, 1859, p. 427.

† Milne Edwards, "Leçons de physiologie," etc., tome i., p. 237.

‡ Lehmann, "Physiological Chemistry," American edition, vol i., p. 548.

* In order to ascertain whether this specimen of blood contained what would be considered as the normal quantity of organic constituents estimated by the old method, these were evaporated to dryness and carefully weighed, with the following result, which it will be seen corresponds with that generally obtained:

Fibrin.....	2.50 parts per 1,000.
Albumin.....	71.53 " "
Globules.....	125.00 " "

The proportion of albumin in the serum was 82.07.

of the system and in different animals, which considerations, indeed, would be beyond the scope of this paper; but the few facts I have collected go to confirm some of the observations which have already been made upon these points. It has been often observed that the blood of the ox is much richer in fibrin than that of the human subject; the former containing 5 to 6 parts per 1,000 dry, while the latter contains but 2 or 3. This difference is shown in the preceding analyses, where the blood of the ox is found to contain 14.52 to 16.27 parts of moist fibrin, human blood containing but 8.82 parts. The analyses also show a greater quantity of fibrin in the two specimens of blood of the female than in the blood of the male. In the observations of others, the quantity has not been found to vary much in the sexes. In this instance, neither of the specimens from the female can be taken as perfectly normal; as in Examination III. the subject was plethoric, and in Examination IV. she had been taking sulphate of magnesia and was somewhat anemic.

The albumin was found to vary considerably in the specimens of human blood, being more abundant in the blood of the male in Examination I. than in the female in Examinations III. and IV., but less in the blood of the male in Examination II. than in the female in Examination III. There are not here sufficient data to lead to any conclusion in regard to the variations of albumin in the sexes. In the blood of the ox the albumin was much less than in human blood.

The quantity of globules was found to be greater in the male than in the female. This has been noticed by all observers who have directed their attention to this point, and is, perhaps, one of the most characteristic of the differences between the blood of the male and of the female. One of the females was slightly plethoric, which caused the globules to mount up nearly to the standard in the healthy male. This condition of plethora, according to Andral, is dependent almost entirely upon an increase in the globules. The difference in this respect between the blood of the female who was slightly plethoric, and the other, who was somewhat anemic, is very marked; in the former the globules are 484.51 and in the latter, 382.95. The blood of the ox was found to be very rich in globules.

In conclusion, I may say that I have not attempted to settle the normal constitution of the blood, much less to follow out the variations to which it is subject. This would require a largely extended series of observations. But, considering a proper idea of the condition of existence of the organic ingredients of great importance to the physiologist and physician, I have endeavored to study this fluid from a physiological point of view; and with the ideas I have been led to entertain on this subject, it seemed that a new method of analysis which would give real proportions of these principles was indispensable. My object has been merely to settle upon some rational and simple process, leaving its extended applications to be made in the future. The process I have described seems to me sufficiently accurate for all practical purposes; and it is so easy of application that I can not but indulge the hope that others may be led to cultivate this interesting and fruitful field of inquiry.

XIV

EXPERIMENTS UNDERTAKEN FOR THE PURPOSE OF RECONCILING SOME OF THE DISCORDANT OBSERVATIONS ON THE GLYCOGENIC FUNCTION OF THE LIVER

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WHEN it was announced by Bernard, in 1848, that he had discovered a new and important function of the liver, there being in this organ a constant production of the same variety of sugar that had long been recognized in the urine of diabetic patients, the great physiological and pathological importance of the discovery, attested, as it was, by experiments which seemed to be absolutely conclusive in their results, excited the most profound scientific interest. During the present century, indeed, there have been few physiological questions which have attracted so much attention; and the observations of Bernard were soon repeated, modified and extended by experimentalists in different parts of the world. In 1857 Bernard discovered a sugar-forming material in the liver, analogous in its composition and properties to starch; and this seemed to complete the history of glycogenesis.

I do not propose at this time to give an extended review of the experiments which have been made in different parts of the world with the view either of confirming or overthrowing the theory advanced by Bernard, but shall discuss the two opinions which are now most prevalent in English and French physiological literature. These two opinions are the following:

Those who accept the experiments of Bernard as conclusive assume that the substance of the liver and the blood in the hepatic veins always contain sugar. This sugar is believed to be formed in the so-called hepatic cells, from

the glycogen contained in them, and to be taken up by the blood as it passes through the liver, existing in the hepatic veins, the ascending vena cava and the right side of the heart. It usually disappears from the blood in its passage through the lungs. Sugar is believed always to exist in the liver, the blood of the hepatic veins and of the right side of the heart, independently of the kind of food used. In the carnivora the blood of the portal system never contains sugar when the animal is confined to a diet of nitrogenous and fatty matters; but sugar is found none the less invariably in the liver and in the vascular system between this organ and the heart.

Others have accepted the view advanced by Dr. Pavy, of Guy's Hospital, who professes to have demonstrated that neither the liver nor the blood circulating between the liver and the heart ever contains sugar during life; but that the sugar which has been found in these situations is the result of a post-mortem change of the glycogenic matter, or as it is called by Dr. Pavy, the amyloid matter of the liver.

These two opposite views are supported by experiments which seem to be conclusive; yet it is evident that, if the observations in both instances are entirely accurate, they must prove precisely the same fact. It was in the hope of harmonizing these discordant opinions, that I undertook some modifications of the experiments of Bernard and Pavy. I shall not discuss the accuracy of the methods employed by these observers but intend merely to follow out a train of reasoning, which seems to me to be fully sustained by experiment and which I believe will lead to a correct interpretation of the apparently opposite results heretofore obtained.

Since the summer of 1858 I have been in the habit of repeating, several times each year, the experiments by which Bernard demonstrated the glycogenic function of the liver, performing the experiments chiefly as class-demonstrations. I have followed most of the modifications of these experiments which have been published by Bernard from time to time and I have almost always confirmed his results in every particular. I have never failed to demonstrate the absence of sugar in the blood of the portal system, when the specimens were taken with proper

precautions from carnivorous animals that had taken neither starch nor sugar into the alimentary canal. I have found it important to apply a ligature rapidly to the portal vein as it penetrates the liver and to make a very small opening into the abdominal cavity in this step of the experiment. When I have detected a trace of sugar in the clear extract from the portal blood of an animal in the condition just mentioned, it has been consequent upon delay in seizing the vein; and I have anticipated the probability of finding sugar from blood, which, under these circumstances, regurgitates from the liver. The necessity of employing these precautions is fully insisted upon by Bernard. I have never failed to find sugar in the blood of the hepatic veins of healthy dogs that had taken neither starch nor sugar into the alimentary canal. In my earlier experiments I never failed to find a great abundance of sugar in the substance of the liver, in dogs under the same conditions. In one instance, however, in the winter of 1859-'60, I failed to find sugar in the liver of a dog that was affected with what is known as "mange"; but I considered this to be due to the peculiar condition of the animal.

On several occasions I have repeated Bernard's experiment of analyzing for sugar, the portal blood, the substance of the liver, the hepatic blood, the blood from the right side of the heart, the substance of the lungs, the blood from the arterial system, and the substance of the muscles, the kidneys and the spleen, all the specimens being taken from the same animal. I have always found that sugar existed only in the substance of the liver, the blood from the hepatic veins, and the right side of the heart and in no other situations; showing, apparently, that sugar is constantly being produced by the liver and is carried by the circulating blood to the lungs, there to be destroyed. On several occasions I have drawn the blood from the right side of the heart of a living animal, by catheterization through an opening into the right external jugular vein (a manipulation which presents no difficulty), and have never failed to find sugar. This experiment I have done without the administration of ether, following the operative procedure described by Bernard.

I have also frequently repeated the experiment of pass-

ing a stream of water through the liver from the portal vein, by which all the sugar can be removed in a short time, and testing the substance of the liver a few hours after, it having been kept in the mean time at a temperature of 80° to 100° Fahr. In this experiment I have always found an abundance of sugar. The glycogen out of which this secondary formation of sugar is supposed to take place, I have extracted and studied after the method proposed by Bernard and have confirmed his observations on this substance in every particular.

In these experiments I have used the various copper tests; viz., Trommer's, Barreswill's and Fehling's, and have made my clear extracts, generally by boiling with an excess of sulphate of soda, but very often by mixing the blood or the watery extracts of the tissues with animal charcoal and filtering.

The theory advanced by Pavy, that sugar is not produced by the liver during life and that when this substance is found in the liver it is the result of post-mortem change of the glycogen (which he calls the amyloid substance), always seemed to me to be invalidated by the experiment of catheterization of the right side of the heart in a living animal without the administration of ether; for in the blood taken under these conditions, the presence of sugar is unmistakable. The admission that sugar is contained in the blood passing out of the liver, when ether has been administered, and the fact that sugar is sometimes produced in the body, in cases of diabetes mellitus (for there are undoubted cases in which sugar is discharged in the urine, when neither starch nor sugar has been taken as food), point to the probable normal production and destruction of this substance in the economy. Sugar can hardly be regarded as a heterologous substance or as a product of decomposition; and it constitutes an important article of food, from the fact that it is consumed in the body in connection with certain of the processes of nutrition.

Dr. Pavy asserts that the liver never contains sugar during life; but that after death, it is formed out of the amyloid substance, and its proportion goes on increasing for a number of hours, particularly when the organ is kept at about the temperature of the body. The ex-

periments of Bernard with a liver washed out with a stream of water also show that sugar may be produced after death.

I was led to perform the following experiments by the fact that of late years, the experiments by which I have been in the habit of demonstrating the glycogenic function of the liver have inclined me to the opinion that the observations detailed by Dr. Pavy are entirely accurate; and that the error consists in his interpretation of the facts. The circumstances which led to this view were the following:

I formerly was in the habit of making my demonstrations of the formation of sugar in the liver upon animals that had been etherized; and then I always obtained a brilliant precipitate from a clear extract of the substance of the liver, boiled with the test-liquid. I performed the experiment in this way before I had acquired sufficient dexterity to seize the portal vein readily and to go through with the necessary manipulations with rapidity. I subsequently made the operation by first suddenly breaking up the medulla oblongata, then making a small incision into the abdominal cavity and seizing the portal vein instantly, following out the remaining steps of the experiment without delay. In this way, although I always found sugar in the blood of the hepatic veins, I frequently failed to obtain a distinct reaction in the extract of the liver; and the more accurately and rapidly the operation was performed, the more difficult was it to detect sugar in the hepatic substance.

It occurred to me, in reflecting upon these facts, that inasmuch as no one has assumed that the actual quantity of sugar produced by the liver is very considerable, and as a large quantity of blood (in which the sugar is very soluble) is constantly passing through the organ, precisely as water is passed through its vessels to wash out the sugar, the sugar might be washed out by the blood as fast as it is formed; and really the liver might never contain sugar in its substance, as a physiological condition, although it is constantly engaged in its production. It is well known that the characteristic elements of the various secretions proper are produced in the substance of the glands and are washed out at the proper time by liquid

derived from the blood, which circulates in the glands during their functional activity in very much greater quantity than during the intervals of secretion. The liver-sugar may be regarded as an element of secretion; and possibly it may be completely washed out of the liver, as fast as it is formed, by the current of blood, the hepatic vein, in this regard, serving as an excretory duct.

To put this hypothesis to the test of experiment, it was necessary to obtain and analyze the liver in a condition as near as possible to that under which it exists in the living organism; and in carrying out this idea, I made the following experiments:

EXPERIMENT I.—A medium-sized dog, full grown, in good condition and not in digestion was held upon the operating-table by two assistants and the abdomen was widely opened by a single sweep of the knife. A portion of the liver, weighing about two ounces, was then cut off and immediately cut into small pieces, which were allowed to fall into boiling water. The time from the first incision until the liver was in the boiling water was twenty-eight seconds. An excess of crystallized sulphate of soda was then added, and the mixture was boiled for about five minutes. It was then thrown upon a filter and the clear fluid which passed through was tested for sugar by Trommer's test. The reaction was doubtful and presented no marked evidence of sugar.

EXPERIMENT II.—A medium-sized dog, in the same condition as the animal in the first experiment, was held upon the table and a portion of the liver excised as above described. The whole operation occupied twenty-two seconds. But ten seconds elapsed from the time the portion of the liver was cut off until it was in the boiling water. It was boiled for about fifteen minutes, made into a paste with animal charcoal and thrown upon a filter. The clear fluid which passed through was tested for sugar by Trommer's test. There was no marked evidence of sugar.

EXPERIMENT III.—A large dog, full grown and fed regularly every day, but not in digestion at the time of the experiment, was held firmly upon the table. This dog had been in the laboratory about a week and was in a perfectly normal condition. The abdominal cavity was opened and a piece of the liver was cut off and thrown into boiling water, the time occupied in the process being ten seconds. Before the liver was cut up into the boiling water, the blood was rinsed off in cold water. The liver was boiled for about seventeen minutes, mixed with animal charcoal and the whole thrown upon a filter.

Immediately after cutting off a portion of the liver and throwing it into boiling water, the medulla oblongata was broken up; a ligature was applied to the ascending vena cava just above the renal veins; the chest was opened, and a ligature was applied to the vena cava just above the opening of the hepatic veins. A

specimen of blood was then taken from the hepatic veins. This part of the operation occupied not more than one minute. A little water was added to the blood, which was boiled briskly, mixed with animal charcoal and thrown upon a filter. The liquids which passed through from both specimens were perfectly clear.

While the filtration was going on, Fehling's test liquid (a mixture of sulphate of copper, neutral tartrate of potash and caustic soda) was made up, so as to be perfectly fresh.

The two liquids were then carefully tested for sugar with this solution. The extract of the liver presented not the slightest trace of sugar. The extract from the blood of the hepatic veins presented a well-marked deposit of the oxide of copper, revealing unequivocally the presence of a small quantity of sugar.

In these experiments I did not attempt to show the absence of sugar in the blood of the portal system; for it would have been difficult, if not impossible, to have demonstrated this and at the same time to have obtained the specimens of liver as rapidly as I desired. The fact that the portal blood in a carnivorous animal that has taken no saccharine or starchy matters into the alimentary canal contains no sugar, I regarded as settled by the experiments of Bernard, which I have repeatedly confirmed. Neither did I attempt to show that sugar exists in the liver when a certain period has elapsed after death; for this fact has been demonstrated by all who have experimented on the subject. I desired only to ascertain whether the liver taken from a living animal, and the change of the glycogen arrested before any sugar has had time to make its appearance, if its formation is post mortem, really contained sugar. A few seconds only elapsed before the liver was cut up into boiling water (which will effectually arrest the transformation of the glycogenic matter), and the presence of sugar in the decolorized extract could not be demonstrated. In Experiment III. particularly, very delicate tests were employed with the greatest care; and although the extract of the liver contained no sugar, the presence of sugar in the blood coming from the liver was unmistakable. This experiment was peculiarly successful; and I could hardly expect to be able to collect the specimens with less delay. Anesthetics were not employed in any of the experiments, and there seemed to be no circumstance that could interfere with the normal character of the specimens examined. The animals were perfectly quiet when the experiments were begun, and

they were operated upon as soon as they were put upon the table, the respiration and circulation being apparently normal.

CONCLUSIONS

Although these experiments are not entirely new, my interpretation of them serves to harmonize, in my own mind at least, the results obtained by Bernard and by Pavy:

I. A substance exists in the healthy liver, which is capable of being converted into sugar; and inasmuch as this is changed into sugar during life, the sugar being washed away by the blood passing through the liver, it is proper to call it glycogen, or sugar-forming matter.

II. The liver has a glycogenic function, which consists in the constant formation of sugar out of the glycogen, this sugar being carried away by the blood of the hepatic veins, which always contains a certain proportion of sugar, and subserving some purpose in the economy connected with nutrition, as yet imperfectly understood. This production of sugar takes place in the carnivora as well as in those animals that take sugar and starch as food; and it is essentially independent of the kind of food taken.

III. During life the liver contains only the glycogen and no sugar, because the great mass of blood which is constantly passing through this organ washes out the sugar as fast as it is formed; but after death or when the circulation is interfered with, the transformation of glycogen into sugar goes on; the sugar is not removed under these conditions, and can then be detected in the substance of the liver.

XV

THE TREATMENT OF DIABETES MELLITUS *

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It would not be possible, within the limits to which this paper is necessarily restricted, to discuss satisfactorily the pathology or even the clinical history of diabetes mellitus, although the disease in question is one of the most interesting as well as obscure affections which the physician is called upon to treat. While the study of diabetes and of its attendant disorders of general nutrition presents difficulties, as regards questions of causation and pathology, that seem almost insurmountable, when attention is once directed to the simple problem of the presence of sugar in the urine, this condition is now easily and certainly recognizable. It is probably true that sugar exists in the urine of a certain number of persons, unattended with symptoms, so that it is detected only by accident or may never be revealed, such persons having no apparent occasion to seek medical advice. In an experience in life insurance examinations extending through a period of nearly thirteen years, I have found a small quantity of sugar in the urine of applicants who supposed themselves to be perfectly healthy; but within the time mentioned, only five such cases have come under my observation. Three of these applicants are now living and are presumably in good health, the sugar in the urine having been noted eight to twelve years ago; one case was lost sight of and one applicant is reported to have died of hemoptysis nine months after the examination of the urine. During the time mentioned; viz., twelve years and nine months, I examined 1,884 persons who supposed themselves to be in good health and nearly always

* Read in the Section on Practice of Medicine and Materia Medica of the American Medical Association, in May, 1884.

made examinations of the urine. All of the applicants, with one or two exceptions, were males. The proportion, therefore, of apparently healthy persons in whose urine I have found sugar is very small (1 in 377); but even this shows that sugar may be present in the urine, either as a transient or an insignificant condition or existing without any of the general symptoms of diabetes.

In the great proportion of cases of diabetes that come under observation, attention has been directed to the condition of the urine by certain general symptoms, such as excessive thirst, persistent polyuria, a sensation of dryness of the mouth and fauces, fatigue after moderate muscular exertion or some slight affection of the external genitals. In a case of diabetes that I have had under treatment for nearly four years, now under observation, the patient first consulted a physician for herpes progenitalis, which led to an examination of the urine. In females, persistent pruritus of the vulva is often the first trouble pointing to the possible existence of diabetes. In several cases I have detected sugar in the urine when pruritus vulvæ was the only trouble complained of by patients. So constant is this symptom, that diabetes should always be suspected when the pruritus persists without any apparent cause and resists ordinary measures of treatment. The pruritus is seldom absent when the proportion of sugar in the urine is considerable.

DETECTION OF SUGAR IN THE URINE.—So far as purely clinical examination of the urine is concerned, the great desideratum is a simple test, easy and rapid in its application, upon which one can rely with absolute confidence. I shall pass over, without discussion or even mention, the different tests employed for the detection of sugar, except the one known as Fehling's. When the Fehling's liquid is properly prepared and carefully used, there can be no error in the results. If a quantity of this test, however, be made and kept for some time, it is liable to change so as to become more or less unreliable. This want of stability in the test-liquid has long been recognized by those accustomed to urinary examinations; and a few years ago I prepared three separate liquids, which I mixed in certain proportions for use as required. Even this did not prove to be entirely satisfactory. Within the last year, two separate liquids have been prepared by Dr. E. R. Squibb, and are kept by him

for sale, in which form the test seems to leave nothing to be desired in the qualities of accuracy and ease of application. The test, as it is now prepared by Dr. Squibb, is simply perfect; but so much depends upon its proper use, that I venture to give an account of its application and the necessary precautions to be adopted. These precautions are simple and demand no special skill; but they often become very important, especially in determining with certainty the absence of sugar.

The two test-liquids are prepared by Dr. Squibb according to the following formulas:

FOR THE SOLUTION OF CUPRIC SULPHATE.—Use purified sulphate of copper, in granular crystals, air-dried. Weigh 277 grains (17.32 grammes) of the salt and dissolve it in about 4 fluidounces (120 cc.) of distilled water, adding about 4 minims ($\frac{1}{4}$ cc.) of pure sulphuric acid. Add distilled water to this solution to make $8\frac{1}{2}$ fluidounces (260 cc.).

FOR THE SOLUTION OF ALKALINE TARTRATES.—Weigh 2 ounces, 391 grains (87.5 grammes) of re-crystallized sodio-potassic tartrate, or Rochelle salt, and dissolve it in about 6 fluidounces (175 cc.) of distilled water. Filter the solution, if necessary, and add it to a clear solution of 386 grains (25 grammes) of caustic soda in about $1\frac{3}{4}$ fluidounces (50 cc.) of distilled water. Add distilled water to this solution to make $8\frac{1}{2}$ fluidounces (260 cc.).

These two solutions are to be kept in separate bottles for use. If they are made with accuracy and mixed together in equal proportions, two hundred grains of the mixture will be decolorized by exactly one grain of sugar, or each cubic centimetre of the mixture will be decolorized by 0.005 of a gramme of sugar. The liquids can therefore be employed for quantitative estimates, although I shall describe the use of the test simply for determining the fact of the presence or absence of sugar.

For use in qualitative analysis, the two liquids may be roughly mixed in about equal proportions in a test-tube or they may be measured accurately and diluted with about an equal volume of distilled water. The latter process should be resorted to in all delicate analyses.

For ordinary use the following process may be employed:

Mix in a test-tube equal volumes of the two liquids so that the mixture will extend in the tube to the length of about an inch.

Bring the mixture to the boiling point and then add to the boiling test a quantity of urine equal to that of the test.

Bring the mixture of the test-liquid and urine to the boiling point and then allow it to cool.

If no distinct and opaque reddish or yellowish precipitate is present when the mixture of test and urine has become cool after the second boiling, it is certain that no sugar is present.

All these precautions are essential; and I have repeatedly examined specimens of urine in which the characteristic precipitate due to the presence of sugar did not occur until one or two minutes had elapsed after the second boiling.

In very delicate testing, take a definite quantity of the copper solution, add an equal quantity of distilled water, add then of the solution of alkaline tartrates a quantity equal to the quantity of the copper solution, and add finally distilled water in the same quantity. When this mixture is boiled, if the test is not absolutely perfect, there will be a precipitate before the urine is added. The mixture, if perfect, may be used in the same way as the simple undiluted mixture of the two solutions.

When sugar is present in the urine, an opaque yellowish or reddish precipitate appears at some time during the process, the promptness of its appearance and its quantity being in direct proportion to the quantity of sugar.

It is often important to be able to determine, at least approximately, the quantity of sugar discharged in twenty-four hours or its proportion per fluidounce. Using the volumetric process, this estimate requires some practice and occupies twenty to thirty minutes; but the "differential density method" recommended by Roberts, is very simple and is sufficiently accurate for ordinary purposes. With a little practice, indeed, it may be employed by intelligent patients.

Two specimens of diabetic urine are taken, about four ounces of each, one for comparison and the other for analysis. To one is added a lump of German yeast, about the size of a filbert, in a bottle with a cork nicked to allow the

escape of gas; and the other specimen is placed in a similar bottle tightly corked. The bottles are then put aside in a warm place, as the mantelpiece in winter or in the sun in summer. In the course of twenty-four hours, fermentation will have been completed in the specimen to which yeast has been added. If the specific gravity of the two specimens is then compared, the fermented specimen will be found much the lighter, from loss of the sugar which has been decomposed into alcohol and carbonic acid. The difference in the density of the two specimens, expressed in degrees of the urinometer, will represent the number of grains of sugar per fluidounce in the urine. For example, if the specific gravity of the fermented specimen is 1010, and the specific gravity of the unfermented specimen, 1040, the urine contains thirty grains of sugar per fluidounce. In this process it is essential to compare the density of the two specimens at the same temperature. If German yeast can not be obtained readily, about a teaspoonful of ordinary baker's or brewer's yeast may be used.

RELATIONS OF THE SPECIFIC GRAVITY OF URINE TO THE PROPORTION OF SUGAR.—It has long been recognized that the specific gravity of the urine bears no definite and constant relation to the proportion of sugar in cases of diabetes. In a case that came under my observation in December, 1883 and has been under treatment until the time of writing (April, 1884) on Dec. 29, 1883, the specific gravity was 1038, with 28.4 grains of sugar per fluidounce. The next day, the specific gravity was 1036 and the proportion of sugar was 9 grains per fluidounce. In another very interesting case now under treatment, I found 4 grains of sugar per fluidounce, the urine having a specific gravity of only 1011½. These remarkable variations in the specific gravity, occurring without any relation to the quantity of sugar, are generally dependent upon the proportion of urea, the absolute quantity of which is often very largely increased in cases of diabetes. I have often found crystals of uric acid as a persistent condition in diabetic urine, sometimes associated with a deposit of oxalate of lime.

The time allotted to me does not permit a discussion of the possible relations of the nutritive conditions connected with diabetes to the excessive elimination of urea or the

frequent presence of crystals of uric acid; but it is very important to remember that urine of a comparatively low specific gravity may contain sugar. Within a week, in another case in which the urine is examined every three or four days, I found a marked sugar-reaction in a specimen of urine with a specific gravity of 1011. I have also repeatedly found sugar in urine of a specific gravity of about 1020, the quantity of urine in twenty-four hours being normal. The fact, then, that the quantity and specific gravity of the urine are normal does not in itself exclude sugar; although, in most cases of diabetes, the quantity of urine is increased and its specific gravity is notably high. In a case of diabetes very minutely reported by Pavy, sugar was found in the urine when the specific gravity of the specimens was, on different occasions, 1010, 1011, 1012 and 1013.* In cases in which diabetes is suspected, the physician is not justified in excluding the disease when he finds no increase in the quantity of urine and a normal specific gravity; and the facts just mentioned show that in all cases of this kind the urine should be carefully tested for sugar.

WHAT CONSTITUTES DIABETES MELLITUS?—A patient with abnormal thirst, dryness of the mouth, suffering from fatigue following slight muscular exertion, progressively losing strength and weight and passing an abnormally large quantity of urine of high specific gravity and containing sugar has the disease known as diabetes mellitus; but the various symptoms just enumerated may exist in greater or less degree or some of them may be absent. In addition to these symptoms, others may exist; such as, abnormal dryness of the skin, deficient perspiration on exercise or in warm weather, pruritus of the vulva, a tendency to furuncles, unusual liability to "take cold," reduction in the general temperature of the body, an excessive appetite, failure of the generative functions, etc., but these are not necessarily present in cases of diabetes.

On the other hand, none of the general symptoms that I have mentioned may be observed; the urine may be normal as regards quantity and specific gravity; but still sugar may exist constantly in small quantity. In such instances,

* Pavy, "Nature and Treatment of Diabetes," London, 1869, p. 288.

which are not infrequently observed, the constant, necessary and invariable symptom of diabetes is present; namely, glycosuria. Strictly speaking, perhaps, patients with no general symptoms, with no increase in the quantity of urine and with urine of normal specific gravity may be said to be affected with glycosuria, but not to have diabetes. In the great majority of cases, however, unless the glycosuria is transient and dependent upon some recognizable or temporary cause, certain of the general symptoms of diabetes will sooner or later become developed, unless the glycosuria is relieved by treatment. Still, even without treatment, persons may live in what seems to be perfect health for years, constantly passing considerable quantities of sugar. I can now call to mind three cases of this kind; and several cases, in which I have found sugar in the urine without any other diabetic symptoms, have passed from under my observation.

I shall have little to say concerning the etiology and pathology of diabetes. The physiological experiments, which began with the discovery of the sugar-producing function of the liver by Claude Bernard, in 1848, have failed, in a great measure, to fulfil the expectation that they would lead to a full comprehension of the pathology of this disease. I believe it to be true that the liver is a sugar-producing organ. The experiments of Pavy, in which he showed that the liver-substance does not actually contain sugar during life were, in my opinion, harmonized with those of Bernard, by experiments made by me in 1869.* In these experiments, I found no sugar in an extract of the liver taken from a living dog and put into boiling water in ten seconds, while sugar was present in blood taken from the hepatic veins. I am convinced that the liver is constantly forming sugar during life; but that this sugar, as fast as it is produced, is washed out of the sugar-producing organ by the blood-current. Experiments have shown, also, that the sugar contained in the food as well as that resulting from the digestion of starch is destroyed in the organism. That the sugar-forming function of the liver may become exaggerated beyond the power of the organism to

* "Experiments undertaken for the Purpose of reconciling some of the Discordant Observations upon the Glycogenic Function of the Liver."—"New York Medical Journal," 1869, vol. viii., p. 373 *et seq.*

destroy the excess thus formed was demonstrated by the remarkable experiments of Bernard, in which he produced temporary glycosuria in animals by mechanical irritation of the floor of the fourth ventricle, by stimulating the pneumogastric nerves or by introducing irritating vapors into the lungs; but although cases of traumatic diabetes occur in the human subject, they are exceedingly rare. No such case has yet come under my observation.

I do not propose, at this time at least, to offer any theory in regard to the causation or pathology of diabetes, the cause of death in the so-called diabetic coma or the supposed development, in certain cases, of acetonemia. The discussion of these points has, up to the present time, been very unsatisfactory. It is well known that patients presenting in a well-marked degree certain characteristic symptoms, in addition to glycosuria, are affected with a very grave disease, the pathology of which is imperfectly understood. The sugar resulting from digestion is in great part discharged in the urine. The nutritive processes are seriously disturbed. The power of resistance to other diseases is impaired; and what is remarkable and quite interesting in its relations to our ideas of the production of animal heat, the failure to consume the carbohydrates seriously affects the power of resistance to cold, and the general temperature of the body is habitually 95° or 96° Fahr., instead of about $98\frac{1}{2}^{\circ}$. This latter point I state upon the authority of many writers; and in a case now under treatment, the temperature in the axilla has constantly been about $96\frac{1}{2}^{\circ}$. As the patient improved, the temperature was increased to a fraction above 97° , but it has not yet reached the normal standard.

Being brought, then, face to face with a disease, very obscure in its pathology and not infrequent in its occurrence, the practical question, to which I intended to devote the main part of this paper, is how far it is amenable to treatment. To this question I shall devote what remains of the time at my disposal.

TREATMENT.—In a course of lectures by Cantani, delivered at the clinical hospital of the University of Naples, in the spring of 1872, there occurs the following statement, italicized by the author:

“Diabetes has become to-day a disease easily and cer-

tainly curable, provided that the treatment (cure) is not begun too late." *

The cases which Cantani details in support of this rather startling statement show certainly most remarkable effects of treatment. Judging from the account of these cases, the general proposition that diabetes is a disease in the main easily and certainly curable is not too decided and absolute. Since I have been engaged in treating cases of this disease, my experience, though not extending over many years, has led me to the conviction that the claim made by Cantani is not entirely extravagant.

In the great majority of cases in which patients will submit to certain measures of treatment so soon as it is established that they are suffering from diabetes, or so soon as glycosuria is recognized, it is possible to effect either a cure of the disease or a removal of most of the characteristic symptoms, with the exception, perhaps, of the occasional appearance of a small quantity of sugar in the urine.

Time does not permit me to discuss fully the treatment recommended by different writers. Cantani relies mainly upon dietetic measures, although he attaches considerable importance to the exhibition of lactic acid and the alkaline lactates. Of course the treatment by eliminating sugar and starch from the diet is by no means novel. Dating from the time of Rollo, it has had the earnest support of Bouchardat, Pavy, Seegen and many others. I desire to state at the outset, that the main and almost the sole reliance of the physician should be upon diet; and that the suppression of starch and sugar should be nearly absolute. Bearing this constantly in mind, in considering the different measures of treatment I shall divide them into dietetic, general, and medicinal.

DIETETIC TREATMENT.—In 1869, a patient was sent to me from Omaha, Neb., whom I found to be suffering from many of the distressing symptoms of diabetes.

On November 20, 1869 he passed 224 fluidounces of urine in the twenty-four hours, with a specific gravity of 1035. The quantity of sugar passed in the twenty-four hours was 18 ounces and 30 grains, and the quantity of urea was 624 grains. I recommended a diet-table by no

* Cantani, "*Le diabète sucré et son traitement diététique*," Paris, 1876, p. 386.

means so rigid as the one I now employ, and he left for home. For several years I heard from this patient, either personally or through his physician in Omaha, from time to time, and he was reported as apparently well but occasionally passing a small quantity of sugar. He continued the diet more or less faithfully for two or three years but took a little bread. About five years after, I was accosted in the street by this patient, who reported himself as feeling perfectly well and giving but little attention to his diet. At this time I did not have an opportunity of examining the urine. The patient has since died; and I heard from his widow that this occurred in August, 1881, his death being immediately due to inflammation of the bowels after a few days' illness. "The diabetes was much improved and troubled him very little."

This case, during the time when I was constantly receiving favorable reports, seemed to me to be quite remarkable; and in 1880, having frequent occasion to recommend a diet for diabetics, I carefully compiled an antidiabetic diet-table, which I have since used constantly in cases that have come under my observation and which I shall present as an appendix to this paper. In preparing this table, my object has been to secure a diet sufficiently nutritious but free from starch and sugar, using as a basis the admirable list given by Bouchardat; * and I have endeavored to adapt the articles and their preparation to the customs of our own country, adding to it, when possible, in order to secure the greatest available variety of food. Selecting, however, every dish known in the culinary art, without reference to the trouble or expense of its preparation, a rigid diet is by no means easy of enforcement. Patients at first have an intense craving for bread; and this desire is so nearly universal that almost all writers on diabetes suggest some substitute for this important article of food. I do not hesitate to say, however, without specifying any one of the so-called antidiabetic breads and flours as especially bad, that all the articles of this kind in our markets are unreliable and most of them fraudulent. I have analyzed, or caused to be analyzed, nearly all of the so-called bran-flours and gluten-flours and have invariably found

* Bouchardat, "De la glycosurie ou diabète sucré," Paris, 1875, p. clxxxvi

large quantities of starch. Two specimens said to be free from starch, which were analyzed with great care by a competent chemist, were found to contain a greater proportion than exists in ordinary wheat-flour. Most of the so-called diabetic breads are pasty, heavy and become extremely distasteful. A patient now under occasional observation, having procured a new bread which was so agreeable to the taste that he took it freely and with relish, imagined that he had found at last an article which would be regarded by diabetics as the greatest boon. This bread was made of flour which contained about 80 per cent. of starch.* The effects of this fraud upon the patient were quite serious. His health had become nearly restored and the sugar had disappeared from the urine. Under the use of the bread the sugar returned and it was several weeks before it disappeared again under a strict diet. In the rigid dietetic treatment bread should be absolutely interdicted; or in case patients should refuse to submit to a strict diet, a small quantity of crust of bread taken with an abundance of butter may be allowed.

A rigid diet, without bread, should be continued until the sugar has disappeared from the urine and all the diabetic symptoms have disappeared. Although many diabetics rebel under this regimen and the execution of this measure demands on their part much self-denial and fortitude, patients may be encouraged to persevere, by the statement that the craving for saccharine and starchy articles is likely to diminish and may almost disappear after a few weeks. I have now under observation and treatment several patients who have actually lost all desire for most of the interdicted articles of food.

In cases in which the treatment is followed by an apparent cure, sugar no longer existing in the urine, a gradual return to the normal diet should be begun about two months after the glycosuria has disappeared; but it is of the greatest importance during this part of the treatment to keep patients, if possible, under constant observation, examining the urine at least once in five or six days. When the sugar disappears, patients may regard themselves as permanently cured and no general symptoms present themselves for

* Ordinary wheaten flour contains about 70 per cent. of starchy matters.

some time after glycosuria has returned under a mixed diet. Several unfortunate examples of this have come under my observation.

GENERAL TREATMENT.—Measures of general treatment are to be directed mainly to promoting the proper action of the skin, which often is harsh and abnormally dry, and to general muscular exercise. Systematic rubbing, as practiced by massage, and Turkish or Russian baths once a week, if not contraindicated by some complicating conditions, are useful. A reasonable restriction in the taking of liquids is quite important in diminishing the quantity of urine. Under dietetic treatment the excessive thirst is almost always relieved; but when this persists, it may often be temporarily met, so far as dryness of the mouth is concerned, by taking small pieces of ice from time to time instead of drinking water. I do not know that any reliance is to be placed upon the use of the various mineral waters that are said to exert a curative influence on the disease. Alcoholic stimulants are to be avoided. I have seen several cases of diabetes in which the disease seemed to be attributable to the abuse of alcohol, especially the habitual and excessive drinking of champagne. In certain cases some kind of alcoholic beverage seems to be necessary to maintain the vital powers. For this purpose, a fairly good, sound claret has seemed to me to be the best form in which alcohol may be taken. Spirits should be interdicted or given very sparingly, and not more than a pint of claret should be taken daily.

Patients suffering from diabetes lose to a certain extent their capacity for sustained mental effort. They should be cautioned, therefore, against excessive intellectual work. Mental anxiety and "worry" over business or other affairs exert a very unfavorable influence on the progress of the disease. In some cases apparently cured I have noted a return of the glycosuria which seemed to be fairly attributable to mental causes. Insomnia rarely demands the use of narcotics and usually is relieved with the other symptoms by the antidiabetic diet.

The various minor complications that are liable to occur can usually be overcome by appropriate treatment. Boils are very common and they are likely to be persistent and annoying. When the tendency to boils is very marked, the

sulphide of calcium is useful, although this agent does not seem to exert a curative influence on the diabetic condition. Sulphide of calcium has been recommended very highly as a remedy controlling the glycosuria; but it often is disagreeable to patients and disturbs digestion. In a few instances in which I have employed it for a considerable time, it has not seemed to affect the discharge of sugar, and I regard it as useful only to combat the furuncular tendency. It is dangerous to rely upon drugs to any extent in the treatment of this disease. Patients willingly put faith in remedies rather than in a rigid diet; but after all, diet is the main and almost the only reliance in treatment.

A very important, and perhaps the most important measure of general treatment is systematic muscular exercise, not carried to the extent of producing excessive fatigue. This may be taken in the form of gymnastics or of outdoor exercise, such as riding or athletic sports; but patients should always be cautioned to avoid "taking cold." If a patient suffering from diabetes can be made to develop his muscular strength by moderate and systematic exercise, not too prolonged and followed by a proper and not excessive sense of fatigue and some perspiration, with a good reaction after bathing and rubbing, much will be gained. This is strongly recommended by all writers upon diabetes.

The diminished power of resistance to cold which exists nearly always in diabetics renders it necessary to enjoin great care to avoid exposure to the vicissitudes of the weather, and the constant protection of the body by warm clothing, especially flannels next the skin.

MEDICINAL TREATMENT.—There is no remedy that exerts a curative influence over diabetes in the absence of proper dietetic measures. Opium, the bromides, sulphide of calcium, various mineral waters and other medicinal agents that have been recommended from time to time have all proved unsatisfactory in practice. Of course it is difficult to estimate the value of drugs in this as in many other diseases, particularly as the physician is not justified, in my opinion, in neglecting to enforce a rigid diet which in itself, in the great majority of cases, exerts a decided influence over the glycosuria and the general symptoms. On theoretical grounds, Cantani recommends lactic acid, taken in

the form of a "lemonade," in small quantities throughout the day. The formula for this mixture is the following:

Pure lactic acid.....	3 iss to 3 v.
Aromatic water.....	3 v to 3 j.
Water.....	Oij.

This remedy is regarded by Cantani as useful in many cases but not essential. I have little experience in its use.

Keeping in mind the small reliance to be placed on the efficacy of drugs not conjoined with dietetic measures, I must bear testimony to the apparent advantage to be derived from the use of the bromide of arsenic, recently proposed by Clemens. While I have not felt justified in using this remedy to the exclusion of an antidiabetic diet, for the reason that the bad effects of an unrestricted diet frequently persist for some time, I have noted very marked effects from Clemens' solution in controlling the discharge of sugar and some of the distressing symptoms, particularly the excessive thirst; so that, aside from simple measures to relieve sleeplessness, constipation or other intercurrent difficulties, I have lately been in the habit of prescribing, in addition to the diet, three drops of Clemens' solution, three times daily, in a wine-glass of water after each meal, gradually increasing the dose to five drops. The following is the formula for this remedy:

"Liquor brom-arsen consists simply of a chemical union of arsenious acid and bromine, dissolved in water and glycerin, in such a manner that two drops represent the twenty-fourth part of a grain of arsenite of bromine."*

In a case of diabetes of more than five years' standing, now under treatment, the patient has been taking Clemens' solution constantly, with the exception of a single week, from Dec. 27, 1882 to April 2, 1884, more than fifteen months, without unpleasant effects. I began with a dose of two drops three times daily, gradually increased to five drops. On May 13, 1883, the urine having been free from sugar with the exception of a trace on two or three occasions for thirteen weeks, I stopped the bromide of arsenic for one week, the antidiabetic diet being continued. At the end of the week sugar was found in large quantity in the urine. The use of the bromide of arsenic was then re-

* "Medical Times," Philadelphia, Dec. 2, 1882, p. 160.

sumed. At the end of the first week the sugar still existed in small quantity. At the end of the second week the sugar had disappeared and there was no return for six weeks. The patient then left the city and committed many indiscretions in diet. Seven weeks later I examined a specimen of urine and found it loaded with sugar, with a specific gravity of 1030. While absent from New York, the patient had indulged in peas, egg-plant, stuffed tomatoes, green corn, ice-cream, charlotte russe, peaches, raspberries, blackberries and melons. On September 20, after returning to New York and resuming a strict diet with the exception of the crust of half a white roll three times daily, the patient improved. The urine on September 20 had a specific gravity of 1031 and was loaded with sugar. The following week the sugar was much diminished in quantity and it disappeared at the end of the second week.

SUMMARY OF TREATMENT.—The more I study the cases of diabetes that have come under my observation, especially those that are now under treatment, in connection with the writings of those who have faithfully followed the dietetic plan, notably Bouchardat and Cantani, the more thoroughly am I convinced that the prognosis in a recent and uncomplicated case of this disease in an adult is favorable, provided, always, that the proper measures of treatment are rigidly enforced. In the hope of convincing the profession that this statement is reliable, I shall, at the risk of what may appear to be needless repetition, give a summary of treatment, with brief statements of the progress of cases that I am now actually observing.

At the outset patients should be impressed with the fact that they are suffering from a grave disorder and that everything depends upon their full coöperation in the treatment, which treatment is essentially dietetic. The diet-table should be carefully studied and the diet regulated and carried out absolutely.

In case a rigid antidiabetic diet does not promptly influence the glycosuria, it may be well to subject a patient to an absolute fast for twenty-four hours and follow this with the antidiabetic regimen. This rather harsh measure is suggested by Cantani. I shall not hesitate to employ it in cases in which it may seem to be required, although no such case has as yet come under my observation.

The various measures that I have mentioned under the head of "General Treatment" should be enforced, especially systematic daily muscular exercise. A moderate system of training on the plan adopted by athletes is useful; and this, if continued, will do much to render a cure permanent after return to a normal diet.

The return to a normal diet should be gradual, and during this time the urine should be examined frequently, the rigid diet being resumed at the first reappearance of sugar in the urine; but all alcoholic excesses, the immoderate use of sweet fruits and any use of sugar should be interdicted at all times. A patient who has once had diabetes is always liable to a return of the disorder. He must lead a thoroughly careful, hygienic and temperate life. In the words of Bouchardat, "you will not be cured except on the condition that you never believe yourself to be cured." *

While I believe that the physician is justified in encouraging patients to expect relief, and even cure, in recent, uncomplicated cases, the diet is all important; and its regulation can not be expected to be perfect without professional aid in its enforcement. A diabetic is never safe from a return of his disease, even when he believes himself to be cured; and under no circumstances should he pass more than a few weeks without an examination of the urine.

The bromide of arsenic, or Clemens' solution, appears to be useful. Patients may begin with three drops three times daily in a little water immediately after eating, gradually increasing the dose to five drops. This may be continued for weeks and months without producing any unfavorable effects; but the administration of this remedy does not supply the place of the dietetic treatment, which should be enforced in all cases. A rigid diet should be continued for two months at least, even in the mildest cases of the disease. It may be necessary in certain cases to continue it for a longer period, even twelve or more months.

There is probably no such disease as intermittent diabetes. In some instances glycosuria occurs during the season of sweet fruits, when they are indulged in excessively,

* Bouchardat, "De la glycosurie ou diabète sucré," Paris, 1875, p. 49.

and disappears when the diet is changed; but these are mild cases of diabetes, excluding those in which a transient glycosuria follows the inhalation of irritating vapors, the taking of anesthetics, etc.

Robust or corpulent persons are more tolerant of the disease than those who are feeble or spare; and the glycosuria yields, in such cases, more readily to treatment.

Diabetes occurs at all ages. Bouchardat mentions a case in an infant of three years, although the disease is rare before the age of twelve. The most unfavorable cases are those which occur before the age of puberty. An adult male presents the most favorable conditions for cure. In old persons, when the disease is of long standing, the dietetic treatment will secure practical immunity from nearly all the distressing symptoms, although the glycosuria may not be entirely removed.

A study of any of the diet-tables recommended will make it evident that those who are able to follow the required regimen, without regard to the cost of articles of food, present much more favorable conditions, as regards the prospect of cure, than persons in straitened or indigent circumstances. Diabetes, however, occurs in all classes and is by no means a rare disease. A hospital devoted to such cases, where the dietetic treatment could be strictly carried out, would be a boon to the rich and poor alike.

CASES.—I have accounts, more or less complete, of fifty cases of diabetes. Certain of these cases have been lost sight of; others were followed out in their histories to a fatal termination; and twelve, exclusive of a few that are reported to be cured, are still under either observation or treatment.

Of these fifty cases, sixteen have been lost sight of, nineteen are either known to be living or are under observation, and twelve have died at periods of between nine months and twelve years after I first examined the urine.

Of the seven patients who are living but whom I do not consider as under observation, one passes sugar constantly and is under an imperfect antidiabetic diet, but is in what may be called fair health; two are reported as cured, although I have not examined the urine for a long time; four I simply know to be living.

The twelve cases that are under observation are instructive as indicating the value and influence of treatment.

CASE A.—The patient, a gentleman thirty-eight years of age, first became aware that he suffered from diabetes mellitus about June 1, 1883. He is five feet five inches in height and weighs one hundred and twenty-nine pounds. A year ago he weighed one hundred and sixty pounds. He suffered from excessive discharge of urine, with increased appetite, thirst, dryness of the mouth, sleeplessness, fatigue on slight exercise, and, indeed, most of the symptoms of diabetes; but a careful physical examination failed to reveal any other disease. At the time I first saw him, he had been taking quinine and various tonic remedies and had been subjected to an imperfect antidiabetic diet. At this time, December 29, 1883, he passed eighty ounces of urine in twenty-four hours, containing in all 3,072 grains of sugar. He was immediately put upon a strict diet, taking no bread, drinking very little, and relieving the thirst temporarily by taking pieces of ice. In addition, he took three drops of Clemens' solution three times daily, and continued to take ten grains of quinine each day. After forty-eight hours of this treatment, his intense thirst and excessive urination disappeared; but he expressed himself as feeling rather weak although generally much better. The effect, however, upon the discharge of sugar was remarkable. He passed, during the second twenty-four hours of treatment, forty-three ounces of urine, and the total quantity of sugar was reduced from 3,072 grains to 387 grains.

I heard from this patient January 19, 1884, and received a specimen of the urine of the twenty-four hours of January 17th. For the twenty days since December 29, 1883, he had maintained an absolute antidiabetic diet, taking no bread. During this time he took three drops of Clemens' solution three times daily. He had gained three-quarters of a pound in weight. He had suffered somewhat from indigestion but was otherwise quite well. "The very large appetite and thirst are very materially lessened." The quantity of urine in twenty-four hours was forty-eight and one-half fluidounces; specific gravity, 1026; absolutely no sugar; there was rather an abundant deposit of amorphous urates with a number of crystals of uric acid. So far as the diabetic condition is concerned, the general symptoms have disappeared as well as the sugar in the urine.

On January 25, 1884, the dose of Clemens' solution was increased to five drops three times daily. The urine was free from sugar. There was no sugar in the urine on January 27 and 29. He was then allowed the crust of half a French roll at breakfast.

On February 4, 1884, I saw the patient again. He had been at home and had committed some slight indiscretions in diet. The urine had a specific gravity of 1030 and contained a small quantity of sugar. The strict diet was resumed.

On February 10, 1884, there was a trace of sugar in the urine.

On February 24, 1884, the patient still under a strict diet and the use of Clemens' solution, there was no sugar in the urine.

The patient went home, feeling perfectly well, and promised to send a specimen of urine in two weeks. At no time since the beginning of treatment was there any excessive quantity of urine.*

CASE B.—The patient is a gentleman fifty-seven years of age, five feet eleven and one-half inches in height, weighing one hundred and seventy-two pounds. He had suffered from diabetes to his knowledge for about one year, with thirst, fatigue after moderate exertion and other mild symptoms. He had been under a moderate antidiabetic diet for some weeks. After he came under my observation, his urine, under a strict antidiabetic diet, was either entirely free from sugar or contained merely a trace, for ten months. He had no symptoms and regarded himself as cured. For about three months he took four drops of Clemens' solution three times daily.

On January 17, 1884, he presented himself, passing a large quantity of urine of a specific gravity of 1027 and loaded with sugar. Having regarded himself as permanently cured, he had returned to his old diet, including sugar, and had stopped the bromide of arsenic for six months. He felt perfectly well but had noticed for some days that he was passing a large quantity of urine. He was again put upon an antidiabetic diet (which I fear was not strictly followed) with six drops of Clemens' solution twice daily. On February 7, 1884 he passed a normal quantity of urine of a specific gravity of 1022, containing but a trace of sugar.

In this case, I can not secure strict attention to the diet and regular examinations of the urine.†

CASE C.—This patient has been under observation since October, 1880. He was at that time fifty-three years of age, five feet eight and one-half inches in height and weighed one hundred and sixty-eight to one hundred and seventy-two pounds. Glycosuria had been recognized a few weeks before he came under my observation; and he had been subjected to an imperfect antidiabetic diet. He was immediately put upon a strict diet, and from October 21, 1880 to May 18, 1881, his urine generally contained no sugar, although there was occasionally a trace. In this case the diet was strictly followed, and the patient soon lost his desire for prohibited articles, even bread.

On May 18, 1881 he was allowed the fruits in season to be taken without sugar. On June 27 he was allowed a little bread. His urine was practically free from sugar until February 17, 1882, with the exception of an occasion on November 5, 1882, when it had a specific gravity of 1029 and contained considerable sugar following a slight excess at table in taking claret and whisky and water.

* On April 29, 1884 I received a specimen of urine from this patient. The quantity in twenty-four hours was said to be about fifty fluidounces. The specific gravity was 1022½ and contained a trace of sugar. The general health was reported as perfect.

† I saw this patient on April 29, 1884, and he reported himself as perfectly well, but I did not have an opportunity of examining the urine.

On February 17, 1882 his urine had a specific gravity of 1026 and contained considerable sugar. He had been living rather freely for some time without committing any actual excesses at table. He moderated his living and was given, in addition to the strict diet, one-quarter of a grain of sulphide of calcium three times daily. From February 17, 1882 to September 1, 1883 his urine was practically free from sugar when examined on ten different occasions, once, only, presenting a mere trace. During the entire treatment he has taken considerable exercise in walking. He took the sulphide of calcium rather irregularly for six months, but it was very disagreeable.

On January 11, 1883 he began to take the bromide of arsenic, which he continued rather irregularly.

On January 23, 1884 his weight had increased to 175½ pounds. Since September 1, 1883 his diet had been practically unrestricted. His urine had a specific gravity of 1021 and contained a small quantity of sugar. He was put on a moderate antidiabetic diet and the dose of bromide of arsenic was increased to five drops. On February 7, 1884 the sugar was still marked in the urine, but he indulged rather too freely in claret at dinner and drank some brandy and soda during the evening. From February 7, to April 3, 1884 the urine had been nearly always free from sugar.

This may be called almost a case of cure. For the greatest part of the time from October, 1880 to April, 1884, three and one-half years, the urine has been practically free from sugar, for some of the time under an ordinary diet. During this period sugar has appeared temporarily and in small quantity, possibly as a consequence of occasional indiscretions in the use of wine, which could not by any means be regarded as excesses in a person in ordinary health.*

CASE D.—This is the case of a lady, rather stout, fifty-nine years of age, who came to me for treatment in December, 1882. The patient has already been referred to in connection with the fact of the existence of sugar in urine of a low specific gravity, (1011½) and the return of glycosuria immediately following the suspension for one week of the administration of bromide of arsenic.

In December, 1880 the patient was in a deplorable condition, suffering from some of the most distressing symptoms of diabetes. She suffered intensely from thirst, night and day, and was forced to pass urine nearly every hour. She also suffered greatly from pruritus vulvæ. Her disease was of five years' standing, and she had been subjected to various forms of treatment, but never to a strict diet. She had consulted many distinguished physicians in this country and in Europe.

On December 16, 1882 she passed 128 ounces of urine, of a specific gravity of 1036, containing twenty-two grains of sugar per

* On April 28, 1884 this patient reported himself as perfectly well. His urine had a specific gravity of 1020½ and contained no sugar. The diet had been not absolutely strict, but was what may be called moderately antidiabetic.

fluidounce, or 2,816 grains in the twenty-four hours. The next day she was put upon a strict antidiabetic diet.

On December 22, 1882 the daily quantity of urine was reduced to fifty-two ounces, with a specific gravity of 1026 and containing eight grains of sugar per fluidounce, or four hundred and sixteen grains in the twenty-four hours. The urine constantly presented crystals of uric acid. The thirst, pruritus and constant desire to pass urine were relieved.

With the exception of one week, this patient took Clemens' solution, two drops three times daily, the dose finally increased to five drops, from December 27, 1882 to April 2, 1884. The treatment during this period consisted of the diet and Clemens' solution, with occasional remedies to act upon the bowels. She has been almost constantly under treatment, and I made ninety-one examinations of the urine up to April 6, 1884. Her urine is now examined regularly once a week.

Under treatment the quantity of sugar in the urine diminished until the glycosuria disappeared January 27, 1883, about thirty days after the first examination. From January 27, 1883 to April 6, 1884, with the exception of about six weeks passed at a watering-place in the summer of 1883, under very unfavorable conditions as regards diet, the urine has either been free from sugar or has contained a very small quantity. The quantity of urine has been normal, and the general diabetic symptoms have never reappeared. She now uses the antidiabetic diet with the crust of one-half of a French roll at each meal, a pint of cream daily and a little fruit in season.

While this can not be called an instance of cure, the fact that the patient lives comfortably and in apparently good health under a diet that is not particularly irksome shows that cases of long standing and presenting very unfavorable features are by no means hopeless. This case presented in a remarkable degree the example of a loss of desire for prohibited articles of food. She now looks forward to eating melons in season, which is about the only decided wish she has expressed for food not suited to her condition.*

CASE E.—The patient in this case is a gentleman about fifty years of age, living in Ohio. I examined his urine May 24, 1878 and November 17, 1881, for some reason not connected with a suspicion of diabetes and found no sugar. On May 4, 1882 I again examined the urine, on account of certain diabetic symptoms, and found a large quantity of sugar. He was at once put on the antidiabetic diet, which he attempted to carry out by himself at his home in Ohio. In January, 1884 he reported that all his symptoms had been relieved and that he suffers nothing unless he commits indiscretions in diet.

* The urine of this patient is examined regularly once a week, and there has been no sugar, with the exception of a trace on one occasion, for twelve weeks. The last examination was made on May 4, 1884, and no sugar was found. With the exception of sugar, the diet has been but little restricted for three weeks. For the last three weeks the patient has been taking about a pint daily of the lactic acid drink recommended by Cantani.

CASE F.—The patient in this case is a gentleman about fifty years of age and of medium muscular and adipose development. Having been suffering for some months from diabetic symptoms, his urine was examined by me on March 22, 1878. I then found a specific gravity of 1022 and a large quantity of sugar. He was at once put upon a moderate antidiabetic diet.

On April 26, 1878 I found the urine normal and the diabetic symptoms had disappeared. Between April 26, 1878 and January 10, 1882 I examined the urine seven times, always finding it normal.

On October 14, 1882 he passed ninety-six ounces of urine in the twenty-four hours, with a specific gravity of 1027 and containing four grains of sugar per fluidounce. His diet for some time had been irregular, and he had depended on various remedies, such as the bromides and the sulphide of calcium. He then began to take the bromide of arsenic, but his diet, though moderately antidiabetic, was still imperfectly regulated. His urine, examined February 20, May 18 and May 28, 1883, contained a small quantity of sugar. On August 15, 1883 I examined the urine and found a trace of sugar.*

This patient suffers very little from diabetic symptoms. I have little doubt that the glycosuria could be arrested by a few weeks of strict dietetic treatment.

CASE G.—The patient is a lady, rather stout, and about seventy-five years of age. Attention was directed to the urine on February 7, 1884, by excessive thirst and urination, with pruritus vulvæ. Before I examined the urine it was reported to me that she was passing it in large quantity, the specific gravity being 1040, and that it was loaded with sugar. Under an antidiabetic diet and the bromide of arsenic, in three days the quantity of urine was reduced to the normal standard and the diabetic symptoms disappeared. I examined the urine on February 13, 19, 28, March 4, 11, 17, 21, 25, 31, and April 5, 1884. The urine, with one exception, presented sugar in small but variable proportions; but its quantity usually was normal, and the specific gravity varied between 1007 and 1020. The urine on one occasion, with a specific gravity of 1010, contained a trace of sugar. On March 17, the urine had a specific gravity of 1007 and contained no sugar. The general diabetic symptoms are now entirely relieved. The only fault in the diet is that the patient takes a quart of milk daily. The progress of this case is quite favorable up to the present time.

CASE H.—The patient is a large and rather corpulent man about sixty years of age. I examined the urine December 27, 1882 and found it with a specific gravity of 1027 and containing a considerable quantity of sugar. He was at once put upon an antidiabetic diet. Under this treatment the glycosuria and other diabetic symptoms disappeared. In July, 1883 he was attacked with hemiplegia,

* From April 5 to May 2, 1884 I made six examinations of the urine. The specific gravity has been between 1012½ and 1020 and a small quantity of sugar has always been noted; but there have been no general diabetic symptoms. The diet has not been rigidly carried out.

from which he has substantially recovered. He was reported in March, 1884 as perfectly well, having returned to the normal diet.*

CASES I, J, K, AND L.—These are cases of patients who are constantly passing sugar in large quantities, under little or no treatment, but who enjoy fair health. In one of these cases the patient obstinately refuses to regulate the diet; and although he suffers but little from diabetic symptoms, he has become greatly reduced in weight and strength within the past two years. A young daughter of this patient, whom I saw repeatedly and who never followed out an antidiabetic diet, died of diabetes about three years ago. Another patient has fair health under a rather irregular diet. He is so situated as to be unable to carry out a strict regimen. The two other patients are large and corpulent men, who pass immense quantities of sugar, with no restriction in diet or in drinking.

Of the fifteen cases of death the reports are generally imperfect. Four are reported as having died of diabetes; one, of diabetic coma, possibly acetonemia; three, of albuminuria; one, of apoplexy; one, of hemoptysis; one, of "inflammation of the bowels"; and in the remaining four cases I have not been able to learn the cause of death.

CASE M.—I have already referred to this case. The patient was a stout, heavy man about forty years of age. I examined him November 20, 1869. He then passed 224 ounces of urine in the twenty-four hours, with a specific gravity of 1035, containing 18 ounces and 30 grains of sugar and 624 grains of urea. He was immediately put upon a moderate antidiabetic diet and returned to his home in Nebraska. I heard from time to time for several years that he enjoyed good health and had little or no glycosuria unless he committed serious indiscretions in diet. He died of "inflammation of the bowels," after a short illness, in August, 1881, nearly twelve years after I first saw him in 1869.

CASE N.—On November 6, 1879 I saw in consultation a lady about fifty-eight years of age, rather spare in figure, who had been suffering for some months from diabetes. At this time the quantity of urine was not notably increased, the specific gravity was 1030 and it contained a small quantity of sugar. The treatment had consisted mainly of an imperfect antidiabetic diet. A more rigid diet was recommended but it was not strictly enforced. On November 10 and 15, 1877 the urine contained a trace of sugar. On November 29, 1877 the urine was free from sugar and the patient was much improved. She left for her home in Cuba, and I saw her again on September 2, 1880, when the urine was still free from sugar. In July, 1881 she was passing large quantities of sugar, and I learned that for several months the diet had been unrestricted and she had eaten sweets and fruits immoderately. She returned to the antidiabetic diet and I found the urine free from sugar, with all the diabetic symptoms relieved, on August 2, 1881. She then returned to her former habits of eating and the urine was found loaded with sugar on September 27 and October 29, 1881.

* This patient died of apoplexy, June 1, 1884.

I learned that she died "of diabetes," never having returned to the antidiabetic diet, in Cuba, in 1882. During the last few weeks of her life she was much prostrated, suffering intensely from boils and carbuncles, which were probably the immediate cause of death.

The diet-table which follows is adapted to those who are able to provide themselves with any kind of food required, without regard to cost, rather than to persons of restricted pecuniary resources; but I have recognized the fact that those who are subjected to an antidiabetic diet should secure every possible variety of food. In making this table I have drawn largely from those already published, particularly the list of permissible articles given by Bouchardat; but after many trials of the so-called antidiabetic flours and bread, I have come to the conclusion as I have already stated, that they are nearly all unreliable. I prefer to make patients abstain entirely from bread or I allow the crust of half a French roll two or three times daily if I can not eliminate bread altogether from the diet. The so-called gluten breads are not only unreliable but they soon become very distasteful. When ordinary bread is allowed, the physician knows, at least, about how much starch is taken.

DIET-TABLE

BREAKFAST.—Oysters stewed, without milk or flour; clams stewed, without milk or flour.

Beefsteak; beefsteak with fried onions; broiled chicken; mutton or lamb chops, kidneys, broiled, stewed, or deviled; tripe, pig's feet, game, ham, bacon, deviled turkey or chicken, sausage, corned-beef hash without potato, minced beef, turkey, chicken or game, with poached eggs.

All kinds of fish, fish-roe, fish-balls, without potato.

Eggs cooked in any way except with flour or sugar, scrambled eggs with chipped smoked beef, pickled salt cod-fish with eggs, omelets plain or with ham, with smoked beef, kidneys, asparagus-points, fine herbs, parsley, truffles or mushrooms.

Radishes, cucumbers, water-cresses, butter, pot-cheese.

Tea or coffee, with a little cream and no sugar. (Glycerin may be used instead of sugar if desired.)

Light red wine for those who are in the habit of taking wine at breakfast.

LUNCH OR TEA.—Oysters or clams, cooked in any way except with flour or milk; chicken, lobster or any kind of salad except potato; fish of all kinds, chops, steak, ham, tongue, eggs, crabs or any kind of meat; head-cheese.

Red wine, dry sherry or Bass's ale.

DINNER.—Raw oysters, raw clams.

SOUPS.—Consommé of beef, veal, chicken or turtle; consommé with asparagus-points; consommé with okra; ox-tail, turtle, terrapin; oyster or clam, without flour or milk; chowder, without milk or potatoes; mock turtle, mullagatawny, tomato, gumbo filet.

FISH, ETC.—All kinds of fish, lobsters, oysters, clams, terrapin, shrimps, crawfish, hard-shell crabs, soft-shell crabs. (No sauces containing flour or milk.)

RELISHES.—Pickles, radishes, celery, sardines, anchovies, olives.

MEATS.—All kinds of meat cooked in any way except with flour; all kinds of poultry without dressings containing bread or flour; calf's head, kidneys, sweet-breads, lamb-fries, ham, tongue, all kinds of game; veal, fowl, sweet-breads, etc., with currie but not thickened with flour. (No liver.)

VEGETABLES.—Truffles, lettuce, romaine, chiccory, endive, cucumbers, spinach, sorrel, beet-tops, cauliflower, cabbage, Brussels-sprouts, dandelions, tomatoes, radishes, oyster-plant, celery, onions, string-beans, water-cresses, asparagus, artichauts, Jerusalem artichokes, parsley, mushrooms, all kinds of herbs.

SUBSTITUTES FOR SWEETS.—Peaches preserved in brandy without sugar; wine-jelly without sugar; "gelée au kirsch" without sugar; "omelette au rhum" without sugar; "omelette à la vanille" without sugar; "gelée au rhum" without sugar; "gelée au café" without sugar.

MISCELLANEOUS.—Butter, cheese of all kinds, eggs cooked in all ways except with flour or sugar, sauces without sugar, milk or flour.

Almonds, hazel-nuts, walnuts, cocoanuts.

Tea or coffee with a little cream and without sugar. (Glycerin may be used instead of sugar if desired.)

Moderately palatable ice-creams and wine jellies may be made, sweetened with pure glycerin; but although these

may be quite satisfactory for a time they soon become distasteful.

ALCOHOLIC BEVERAGES.—Claret, burgundy, dry sherry, Bass's ale or bitter beer. (No sweet wines.)

PROHIBITED

Ordinary bread, cake, etc., made with flour; sugar; desserts made with flour or sugar; vegetables, except those mentioned above; sweet fruits.

ADDENDUM

This diet-table is to be found only in my little book, "Chemical Examination of the Urine in Disease." As it may possibly be copied and used as it appears here, I venture to add this note, indicating the few changes I have made since 1884:

I now exclude celery from the list of salads and permit the meat of the claws only of lobsters.

I no longer recommend glycerin alone as a substitute for sugar, but give the following formula:

Saccharin (300 strength)	3 j;
Glycerin (C. P.)	Oj.

Heat gently to complete solution.

Half a teaspoonful of this preparation, mixed with a little cream, may be taken in a large cup of coffee; two teaspoonfuls will sweeten eight ounces of lemonade; it may be used in any other way as a substitute for sugar.

The ordinary saccharin pellets after a time become distasteful, as they have a slightly acrid impression and soon cease to deceive the palate. I have had patients use the mixture of saccharin and glycerin constantly for years with entire satisfaction and with no disturbance of digestion. (November, 1902.)

XVI

FOUR SELECTED TYPICAL CASES OF DIABETES MELLITUS NOT BEFORE REPORTED *

Published in the "New York Medical Journal" for November 22, 1884.

IN May, 1884 I reported fifty cases of diabetes mellitus to the "Section on Practice of Medicine and Materia Medica of the American Medical Association," and to this report, which is contained in the "Journal of the American Medical Association," July 12, 1884, I refer the Fellows of this Association for full details of the treatment employed. Since this publication I have had under treatment four cases of diabetes, which are typical in many of their characters, illustrating different conditions of the disease and the effects of treatment in patients of different ages.

The first case, which, for my own convenience, I shall designate as Case LIII, illustrates the difficulties met with in treatment when the disease has been allowed to run its course without restraint for a number of months.

CASE LIII.—The patient was an unmarried woman, twenty-two years of age, rather slight in figure when in health, and of medium height. Her parents are living and in perfect health. The family history failed to show any hereditary tendency to this or to any other disease. When in health the patient weighed 140 pounds. This was the weight about three years before she came under my observation. So far as I can judge from the history of the case, the disease must have existed for two years or perhaps longer. In January, 1884 the patient had lost about twenty pounds in weight, had excessive urination, an abnormally great appetite and thirst and suffered from a feeling of exhaustion after moderate exercise. At that time she passed, as was stated, six to eight quarts of urine in the day, which was loaded with sugar. Before the diabetes had become developed, she had enjoyed perfect health with the exception of dysmenorrhœa, which had existed since the

* Read before the New York State Medical Association, November 20, 1884.

age of eighteen. She began to menstruate at the age of thirteen, and at the age of eighteen fell from a wagon, striking on her feet and sustaining no apparent injury at the time. Since this fall, however, she had persistent dysmenorrhœa, suffering intense pain for six or eight hours at every period. She has not menstruated since February, 1884; and in January and February, 1884, she suffered no pain. She was examined in October, 1884, by Dr. James B. Hunter, who found retroversion but advised no interference unless menstruation should return.

When the patient consulted me on August 25, 1884, she presented all the characteristic general symptoms of diabetes mellitus, including excessive appetite and thirst, weariness after slight exercise, some pruritus vulvæ and an increased quantity of urine. Her weight was 92 pounds. During the winter of 1883-'84 and the summer of 1884 she had indulged excessively in starchy matters and sweets, and since January had taken various remedies without experiencing any benefit.

August 26, 1884.—The urine of the twenty-four hours measured 152 fluidounces, was pale, of a sweetish odor and had a specific gravity of 1037. It contained 28 grains of sugar to the fluidounce, giving a discharge of 4,256 grains (8 ounces, 416 grains) in the twenty-four hours. There was no albumin. Microscopical examination revealed the presence of a few octahedra of oxalate of lime with some vaginal epithelium. She was at once put upon a strict antidiabetic diet, all starch and sugar being rigidly excluded, and was ordered to take three drops of Clemens' solution of bromide of arsenic three times daily.

September 1.—The quantity of urine was reduced to 112 fluidounces. The sugar was reduced to $12\frac{1}{2}$ grains to the ounce, or 1,400 grains in the twenty-four hours. The excessive appetite and thirst and the pruritus vulvæ had disappeared. The dose of the Clemens' solution was increased to five drops. She felt better and stronger, and the weight, taken September 3, was increased to 99 pounds.

September 10.—The weight had increased to 103 pounds, and the quantity of urine was reduced to 96 fluidounces, with a specific gravity of 1023.5. The total discharge of sugar for the day was 1,152 grains. The urine, however, presented a trace of albumin. The treatment was continued, with the addition of two grains of quinine three times daily. She had slight uterine pains on September 8, 9, and 10, this being the time in the month when her periods occurred, but there was no menstruation. There was no unusual thirst and the appetite was normal. She bore the strict antidiabetic diet very well.

September 24.—The weight had slightly decreased, being reduced to 101 pounds. The quantity of urine was 80 fluidounces, with a specific gravity of 1025 and containing in all 800 grains of sugar. Since September 10 she had been losing strength as well as weight. The treatment was continued, with the addition of one-quarter of a pint of cream and a tablespoonful of whisky twice daily.

October 10.—The weight was reduced to 96 pounds. The quantity of urine was 80 fluidounces, with a specific gravity of 1023 and containing in all 720 grains of sugar. The patient had followed the treatment, dietetic and medicinal, most faithfully. She had taken, for about four weeks, griddlecakes made of Hecker's farina, which contains only one or two per cent. of starch (?). Notwithstanding the rigid diet, however, I had been unable to reduce the quantity of sugar below 9 or 10 grains to the fluidounce of urine, or 700 to 800 grains in the twenty-four hours, and the strength and general health showed no improvement since September 24. I decided to try to arrest the discharge of sugar by an absolute fast of twenty-eight hours—a method recommended by Cantani. To this plan the patient cheerfully assented. She accordingly fasted from 8 A. M., October 10, to 12 M., October 11, remaining in bed most of the time and taking nothing but water. The urine passed at the close of the fast contained two grains of sugar to the fluidounce; but it presented oxalate of lime, a small quantity of albumin and a few small granular casts. She bore the fast very well, had a good appetite the next day and for several days felt better than she had for weeks. Following the fast the former treatment was resumed.

October 15.—The quantity of urine was somewhat reduced. Its specific gravity was 1030 and it contained 9 grains of sugar to the fluidounce. There was still a little albumin with a few granular casts. The patient left for her home in Georgia on the following day. She was in much better general health than when I first saw her on August 25, but I had found it impossible to arrest the discharge of sugar.

My prognosis in this case is not entirely favorable. It is probable that the excessive indulgence in sweets and in starchy articles of food for several months during the height of the disease has rendered the glycosuria uncontrollable beyond a certain point. Her present safety undoubtedly lies in an antidiabetic diet, and a return to sweets and starch would probably be promptly followed by a return of all of the grave symptoms of the disease.*

The following case is in striking contrast to the one just recited:

CASE LV.—The patient was a young girl, of medium height and development, fifteen years of age. Her father and mother are living and in good health and there is no hereditary tendency to disease. A sister of the patient died at the age of nineteen, probably of diabetes mellitus. The patient began to menstruate at the

* I received a letter from the father of this patient, dated November 2, 1884, stating that "she arrived safely without detention, and bore the fatigue of the trip astonishingly well. She is, I think, evidently stronger and better than when she first placed herself under your treatment."

age of thirteen and has menstruated regularly since that time. She was in perfect health up to January, 1884, when she began to lose flesh slightly and was "ailing" for a few weeks. She soon improved in general health and was apparently well until the middle of August, 1884, when she was found to be passing about two quarts of urine daily, the specific gravity of which was said to be 1052. Since that time she has been on a moderately restricted diet and has taken various remedies. She suffered somewhat from thirst during August and September. Her urine was found sometimes to contain a little sugar and sometimes was free from sugar.

October 8, 1884.—I made a thorough physical examination of the patient and found no disease. The urine was rather less in quantity than normal, had a specific gravity of 1031 and contained no sugar. The only abnormal condition of the urine was the presence of a large number of octahedra of oxalate of lime. The diet had been moderately restricted. I ordered that the diet be unrestricted for twenty-four hours.

October 10.—After twenty-four hours of unrestricted diet, the quantity of urine was slightly increased. It had a specific gravity of 1036.5 and contained 31 grains of sugar to the fluidounce. There were none of the characteristic general symptoms of diabetes. I ordered a strict antidiabetic diet, three drops of Clemens' solution of bromide of arsenic three times daily, the dose to be gradually increased to five drops, and a pill of one-quarter of a grain of codein and one-twelfth of a grain of podophyllin at night, to relieve constipation should it be troublesome. The patient then left for her home in Virginia.

October 16.—I heard from this patient and received a specimen of urine. The treatment had been followed strictly. She had felt perfectly well since her return to Virginia and was passing urine in normal quantity. The urine had a specific gravity of 1015 and contained no sugar.

In this case the glycosuria seemed to be easily controllable. After examining the urine I wrote to the friends as follows:

"I suggest that the dietetic and other measures of treatment be strictly followed until the middle of December. If, at the end of that time, the urine should continue free from sugar, the patient may begin to eat a little bread and gradually return to the usual diet, except that she should never eat sugar or sweets. The urine should be examined from time to time while she is in process of returning to the normal diet."

My prognosis in this case is favorable. With proper attention to the diet I should expect a cure; but it will be necessary to examine the urine occasionally for a long time in order to detect, at the earliest moment, any tendency to a return of the glycosuria.

CASE LI.—This patient was a robust man, unmarried, thirty-four years of age, 5 feet 7 inches in height and weighed 177 pounds. He had always eaten largely of bread and sweets. For several weeks he had a moderate increase in thirst and had not been "feeling very well." His urine had been examined and it was said to contain sugar. His previous health had been good. He had occasionally committed sexual excesses.

I examined this patient on April 8, 1884 and found no disease. The urine was somewhat less in quantity than normal, with a specific gravity of 1035 and was turbid with urates. It contained no sugar. During the day on which this urine was passed the patient had abstained from bread and sweets.

April 10, 1884.—I examined a specimen of the urine passed during the day, the diet having been unrestricted. It had a specific gravity of 1026 and contained a small quantity of sugar.

June 2.—Since April 10 the patient had followed a strict anti-diabetic diet and had taken three drops of Clemens' solution of bromide of arsenic three times daily. His urine had a specific gravity of 1030, was normal in quantity and contained no sugar. The patient felt perfectly well, but his weight had been reduced to 167 pounds. The dose of Clemens' solution was increased to five drops.

July 16.—The patient was still perfectly well, the diet was not irksome and the urine was normal, free from sugar and had a specific gravity of 1024. The weight had been reduced to 161 pounds. The treatment was continued.

August 1.—The patient continued well, but the weight was reduced to 159 pounds. The urine was normal, free from sugar and had a specific gravity of 1029. The treatment was continued.

August 14.—The patient continued well and the weight had increased to 161 pounds. The urine contained no sugar and had a specific gravity of 1026.

August 20.—The patient continued in the same condition. The weight was 157 pounds and he looked and felt in perfect health. The urine contained no sugar and had a specific gravity of 1031. The patient then passed from under my observation. The Clemens' solution was stopped and he was instructed to gradually return to a normal diet, but never to eat sugar or sweets and to carefully abstain from excesses of any kind.

In this case the glycosuria was readily controllable and an apparent cure was effected.

The fourth case is that of a man, fifty-nine years of age, in whom the disease, although of at least a year's standing, yielded promptly to treatment.

CASE LII.—The patient, a married man, fifty-nine years of age, was 5 feet 8½ inches in height and weighed 227 pounds. He was robust, had always enjoyed good health and had been rather a free liver, but without excesses of any kind. The family history gave no evidence of hereditary tendency to disease. For the nine months

previous to the time when he came under my observation he had suffered from excessive urination, annoying thirst, abnormal weariness and impairment of appetite. During this period he had lost about twenty pounds in weight.

August 11, 1884.—I examined a specimen of the urine. Its quantity in twenty-four hours had not been measured but was undoubtedly excessive. It had a specific gravity of 1023 and contained considerable sugar with abundant uric acid crystals. He was at once put upon a rigid antidiabetic diet, with three drops of Clemens' solution of bromide of arsenic three times daily.

August 19.—The general diabetic symptoms had entirely disappeared. The urine was normal, with a specific gravity of 1020 and free from sugar. The weight was unchanged at 227 pounds.

August 26.—The patient felt perfectly well. The urine had a specific gravity of 1012.5 and was free from sugar. The dose of Clemens' solution was increased to five drops.

September 28.—The patient continued to feel perfectly well. The urine had a specific gravity of 1030 and was free from sugar. The weight had increased to 235 pounds. The Clemens' solution was stopped and the patient was allowed to eat a little bread.

October 11.—The patient felt that he was entirely cured. His weight was 233 pounds. The urine was perfectly normal, had a specific gravity of 1020 and was free from sugar. He was directed to follow a reasonable diet, not abstaining entirely from starchy matters, but avoiding sugar and sweets. He was directed to have his urine examined again in about six weeks.

The limited time at my disposal prevents me from giving the diet-table for diabetics and other details of treatment, which would be merely a repetition of what is contained in my paper on the "Treatment of Diabetes Mellitus," published in the "Journal of the American Medical Association," July 12, 1884, and in the sixth edition of my little book on the "Chemical Examination of the Urine in Disease." The diet-table is very varied and is not difficult to follow, the greatest hardship to patients being deprivation of bread. It is a curious fact, however, that after following a strict diet for two or three weeks, diabetics lose their craving for many prohibited articles of food, and the diet becomes by no means irksome. The patients, in all of the cases here reported, were in good circumstances and both willing and able to follow strictly the prescribed diet.

In presenting an account of these four typical cases to the Association, I have purposely put the unfavorable case first. This is the second case that I have met with in which, patients being willing to submit absolutely to treatment, I have not been able to arrest the glycosuria. In this case,

for many months the patient indulged inordinately in sweets; and the disease, which was complicated with albuminuria, had become so thoroughly confirmed that although the general symptoms were controlled, even total abstinence from food did not remove the sugar from the urine after the first week of treatment.

XVII

LITHIUM CARBONATE AND SODIUM ARSENATE DISSOLVED IN CARBONIC ACID WATER IN THE TREATMENT OF DIABETES MELLITUS

Published in "The Medical News" for July 9, 1887.

At a recent meeting of the Therapeutical Society of Paris, Dr. Martineau made a brief communication in which he stated that for several years he had treated cases of diabetes mellitus with a solution of lithium carbonate and sodium arsenate in ordinary carbonic acid water, to the exclusion of every other medicinal remedy and with a moderately strict antidiabetic diet. Dr. Martineau claimed that he had cured sixty-seven out of seventy cases of arthritic diabetes by this method of treatment, which he had borrowed from a practitioner now dead, the late Prof. Rouget, of Paris. The communication was discussed by Dr. Dujardin-Beaumetz and others, who regarded the method as so simple and, to say the least, innocuous, that it was worthy of trial.

The preparation recommended by Dr. Martineau was the following.* Into an apparatus such as is commonly used in Paris for making carbonic acid water, are put twenty centigrammes of lithium carbonate and a tablespoonful of a solution of twenty centigrammes of sodium arsenate in five hundred grammes of distilled water. The quantity of

* "Bulletin et mémoires de la société de thérapeutique," Paris, 30 mars, 1887, 18e année, No. 6, p. 41.

Reduced to the English standard the formula would be about as follows :

Lithium carbonate.....	3 grains.
Sodium arsenate	1 $\frac{1}{6}$ grain.
Carbonic acid water.....	2 pints.

This formula has been published in a number of medical journals. In some it is stated that a teaspoonful of the solution of sodium arsenate is used instead of a tablespoonful. This error arises from a faulty translation of "cuillerée à bouche," which means a tablespoonful. The term for a teaspoonful is "cuillerée à café."

carbonic acid water used is about one litre. This quantity is to be drunk by the patient during each day, either by itself or mixed with ordinary wine at meals.

The simplicity of the proposed remedy led me to make an effort to test its efficacy in certain obstinate cases under treatment for diabetes. I endeavored first to have the agents introduced into the ordinary siphons of soda water prepared and sold in New York; but the manufacturers were unwilling to do this and I was forced to adopt some other method of preparation. It was finally suggested to me to put up the preparation in ordinary beer bottles with patent stoppers which could be replaced after using a certain quantity. This was done, two of these bottles making the equivalent of the quantity administered daily by Dr. Martineau.

I was not prepared to make a trial of the remedy before the middle of April and have used it since then in but three cases—a time too short, and a number of cases too small to admit of anything like definite conclusions. However, in the hope of inducing others to make similar trials, I venture to present the imperfect results of my own brief experience.*

CASE LXXXV.—An unmarried lady, fifty years of age, weighing 115 pounds. Her weight in health was 140 pounds. The disease was recognized six months before she came under my care.

March 11, 1886.—The general diabetic symptoms were marked, and the urine contained $2\frac{1}{2}$ grains of sugar per ounce. The patient was put on an antidiabetic diet, according to my published diet-table,† with Clemens' solution of bromide of arsenic, five drops three times daily. March 19 the quantity of sugar was 7 grains per ounce; March 26, 14 grains; April 2 there was no sugar; and April 7 no sugar. From March 26 to April 7 the diet was absolutely antidiabetic, no bread being taken.

June 17.—The urine had been free from sugar since April 2 under the antidiabetic diet. The quantity was normal and the body-weight had increased by four pounds. The patient expressed herself as feeling "nearly well."

July 28.—The diet for several weeks had been very imperfect, the diabetic symptoms had returned, and the urine contained 24

* The numbers of these cases are made to correspond with the numbers in my book of records.

† "Journal of the American Medical Association," July 12, 1884, and "Manual of Chemical Examination of the Urine in Disease," sixth edition, New York, 1884, p. 85. See also p. 346 of this volume.

grains of sugar per ounce. From this date until April 15, 1887, sugar was found in the urine at every examination, the quantity apparently varying with the diet. During this time I made ten examinations. The general diabetic symptoms were much diminished in prominence although they were distinct. The body-weight did not undergo much change.

April 15, 1887.—The daily quantity of urine was 45 ounces containing $20\frac{1}{2}$ grains of sugar per ounce.

April 16.—With no change in general treatment, the patient was put on the solution of lithia and arsenic, about two pints daily.

April 26.—The quantity of urine was 37 ounces containing 8 grains of sugar per ounce.

May 4.—The diet had been relaxed. The quantity of urine was 52 ounces containing 18 grains of sugar per ounce.

May 12.—The diet had been more rigid. The quantity of urine was 32 ounces containing 6 grains of sugar per ounce.

May 29.—The diet had been imperfect. The quantity of urine was about 40 ounces containing $24\frac{1}{2}$ grains of sugar per ounce.

On May 12 there was some swelling of the eyelids and the quantity of the solution of lithia and arsenic was reduced one-half. On May 14, 15 and 16 the lithia and arsenic were omitted.

The patient was weak and depressed when the treatment with lithia and arsenic was begun. On May 23, about five weeks after, she felt much better and stronger, with a gain of two or three pounds in weight.

With the exception of the indefinite statement by the patient that she felt better in spirits and stronger, the lithia and arsenic seemed to have produced no marked effects. This patient is peculiarly susceptible to starchy and saccharine articles of food. Under measures of treatment that had been very beneficial in other cases, she has lately shown little or no improvement; and the most favorable view to take of the case is that the disease, under proper dietetic treatment, may not progress rapidly.

CASE XCIII.—A gentleman, sixty-one years of age, 5 feet $5\frac{1}{2}$ inches tall, weighing 157 pounds. The disease was recognized fourteen years ago.

November 19, 1886, the patient came under my care. The quantity of urine was 90 ounces containing 19 grains of sugar per ounce. The diet had been very imperfect, milk and grapes having been taken freely. He was put upon a strict antidiabetic diet, with Clemens' solution, five drops three times daily, and one and a half ounces of whisky three times daily. I saw the patient but once and heard of the progress of the case from time to time from his physician in the country.

April 6, 1887.—The patient had not been doing well. He had lost thirteen pounds in weight; the appetite had become very poor and there was great suffering from pains about the chest and in the limbs.

April 20.—The general condition was about the same but the quantity of urine was normal with $6\frac{1}{2}$ grains of sugar per ounce.

The patient was then put upon the solution of lithia and arsenic, two pints daily.

May 11.—The general condition was about the same but the quantity of urine was reduced to 40 ounces and it contained no sugar.

May 19.—It was reported to me that the general condition of the patient was better and that he was stronger. No report was made of the condition of the urine.

CASE XCV.—A married lady, sixty-three years of age, of medium height, weighing 155 pounds. At the present time she has been under my care for a little more than three months. The disease was recognized twelve years ago. In health the patient weighed about 200 pounds.

February 9, 1887.—The general diabetic symptoms are well marked. The quantity of urine is excessive and it contains 23 grains of sugar per ounce. The patient was put upon the anti-diabetic diet, with Clemens' solution, five drops three times daily.

February 14.—The quantity of urine was normal and it had so continued up to this date. The quantity of sugar was 13 grains per ounce. The diabetic symptoms had disappeared.

April 4.—The urine has been examined regularly once a week and the quantity of sugar has been gradually reduced to one grain per ounce. The appetite became very poor about a week ago, and insomnia was very troublesome, with shooting pains over the liver.

April 17.—The patient was put upon the solution of lithia and arsenic, two pints daily.

April 25.—The quantity of urine was about normal and it contained no sugar.

May 17.—The general condition has improved. Since April 25 the urine has contained about one grain of sugar per ounce. Within the past eight months the patient has lost fourteen pounds in weight.

May 24.—The general condition of the patient is much improved. The quantity of urine is normal and it contains about one grain of sugar per ounce.

The general result of the observations on the three cases reported is quite indefinite. The effects of the solution of lithia and arsenic were not well marked, and the slight improvement under its use in Cases XCIII. and XCV. might have been due to other causes. I shall, however, continue the remedy in these three cases and employ it in other cases until I shall have given it a fair trial; but I do not feel that it would be prudent in any case to relax the dietetic treatment.

With other so-called specifics for diabetes mellitus I have had some experience.

I have given calcium chloride in a number of cases, with entirely negative results.

In several cases I have used jambol, also with negative results.

I have never given opium, except for the relief of pain and insomnia; but in cases in which it has been used it has been well tolerated.

I nearly always prescribe at first Clemens' solution of bromide of arsenic. This remedy does no harm, and in many cases it seems to exert some control over the thirst, polyuria and the quantity of sugar in the urine.

I invariably interdict the use of milk and skim milk. In a number of cases in which it has been taken by patients on their own responsibility, I have observed that it promptly induced thirst, polyuria and an immense increase in the discharge of sugar. In some instances in which my published diet-table has been copied, milk has been added. This addition, it seems to me, is most unwarrantable; and the use of milk more than counteracts the beneficial results to be expected from the antidiabetic diet properly carried out.

For the past three years I have recommended a gluten bread which at first contained between two and five per cent. of starch. Within a year, however, it has seemed to act unfavorably. I have lately had a number of analyses made of this bread, and it has been found to contain about thirty per cent. of starch. Within the last two months I have abandoned its use, although this has greatly increased the difficulties of dietetic treatment.

I have not been able to study the details of the seventy cases mentioned by Dr. Martineau, sixty-seven of which he reported as cured.*

The experience of all who have followed out any considerable number of cases of diabetes teaches that the glycosuria nearly always returns under a careless diet; and my own experience is no exception to this general rule. That such an exception should have occurred in the experience of Dr. Martineau would, indeed, be remarkable.

Including the three cases already briefly reported, I have now under observation and treatment ten cases which I have followed for variable periods. It may be interesting

* A brief account of three cases, treated by Dr. Martineau, is given in the "Therapeutic Gazette," Philadelphia, May 16, 1887, p. 330.

to compare seven of these cases with the three treated with the solution of lithia and arsenic.

CASE LXXXIII.—A gentleman, fifty-eight years of age, 5 feet 7 inches tall, weighing 156 pounds. I began the treatment of this case January 17, 1886. The disease had been recognized four years before. The patient had been under the care of an eminent English physician, who gave the opinion, after two or three years of treatment, that the disease would never be entirely cured.

January 17, 1886.—The diabetic symptoms were distinct but slight. The patient had been under a moderately strict antidiabetic diet. The quantity of urine was 60 ounces containing $2\frac{1}{2}$ grains of sugar per ounce. The patient was put upon an absolute antidiabetic diet, without any bread, for two days, and Clemens' solution, three drops three times daily, the dose to be increased in five days to five drops. Two days after, the urine was free from sugar. The patient has continued to be perfectly well in every way up to the present time, being very actively engaged in business.

From January 17, 1886 to May 22, 1887 the urine has been examined twenty-seven times. On December 19, 1886 a trace of sugar was found, this being the only examination in which the urine was not free from sugar. The diet was strict, antidiabetic bread being used for the first three months. Since then, while the patient has been careful, the diet has been rather liberal and the patient has not suffered any serious privation.

CASE LXV.—A gentleman, forty-one years of age, 6 feet tall, weighing 205 pounds. The disease had been recognized six months and the patient had lost about forty pounds in weight.

April 22, 1885.—The patient had the usual diabetic symptoms in a marked degree. The quantity of urine was excessive and it contained 21 grains of sugar per ounce. The patient was subjected to essentially the same course of treatment as detailed in Case LXXXIII. In four days the urine was found free from sugar and the diabetic symptoms had disappeared. Between April 22 and December 22, 1885 the urine was examined thirty-one times. August 10, the urine contained 9 grains of sugar per ounce; September 1, no sugar; December 10, $3\frac{1}{2}$ grains of sugar per ounce; December 22, no sugar. On the two occasions when sugar was found, its presence was probably due to indiscretions of diet, and it promptly disappeared under a strict regimen. After the first two months of treatment the diet was but little restricted. Since December 22 I have seen the patient casually from time to time and he has reported himself as perfectly well.

CASE XCI.—A gentleman, fifty-six years of age, 5 feet 8 inches tall, weighing 166 pounds. Twelve years ago he weighed 200 pounds. Sugar was recognized in the urine eight years before the patient came under my care.

October 14, 1886.—The general diabetic symptoms are slight. For the past eight years the patient has been under a very imperfect antidiabetic diet, and so far as I can learn, the presence of sugar in the urine has been constant. The urine is now normal in

quantity and contains $25\frac{1}{2}$ grains of sugar per ounce. The patient was put upon essentially the same course of treatment as in Cases LXXXIII. and LXV. On October 21 the urine contained $13\frac{1}{2}$ grains of sugar per ounce; on October 26, 11 grains per ounce.

October 29.—The patient was subjected to an absolute fast of thirty-six hours, after the method proposed by Cantani,* taking during that time nothing but water. The fast was borne very well, and on the day following the patient expressed himself as "feeling as well as he had felt in ten years." The quantity of urine during the last twenty-four hours of the fast was 25 ounces and it contained no sugar. The ordinary antidiabetic diet was then resumed. October 31, the urine contained 13 grains of sugar per ounce; November 3, 10 grains. From November 9 to 20, there was no sugar. On February 23, 1887 I heard from the patient. His urine had been repeatedly examined and no sugar had been found. He reported that his "general health had been very good."

CASE VI.—A gentleman, about sixty years of age, 5 feet 6 inches tall, weighing 185 pounds. From March 22, 1878 to February 24, 1885 I had repeatedly examined the urine of this patient while he was partly under the care of the late Dr. Austin Flint. From April 21, 1878 to January 10, 1882 the urine was free from sugar. From October 14, 1882 to February 24, 1885 the urine had generally contained sugar, sometimes in large quantity.

December 13, 1886.—The patient came under my direct care. The quantity of urine was about normal and it contained 18 grains of sugar per ounce. The patient was languid and easily wearied but had no abnormal thirst. He was put upon the usual treatment and took no bread. On December 19 he was much improved. The urine contained $7\frac{1}{2}$ grains of sugar per ounce. The variations in sugar for a few weeks were as follows: December 23, 6 grains per ounce; December 26, $3\frac{1}{2}$ grains; January 1, 1887, a trace of sugar; January 8, a trace of sugar.

May 24, 1887.—The patient had been absent from the city from January 12 to May 4. He now feels perfectly well. On May 4 and 24 the urine contained a faint trace of sugar. Since December 13, 1886 the patient has taken no bread. The antidiabetic diet has been rigidly carried out and the appetite has been tempted by skillfully prepared dishes within the limits of the "diet-table," so that the want of bread has not been a serious privation.†

* Cantani, "Le diabète sucré," p. 402. Paris, 1876.

† In many regards this case is of great interest. Its progress from March 22, 1878 to August 15, 1883 was reported in my article in the "Journal of the American Medical Association" for July 12, 1884, Case F. On April 18, 1871, while the patient was under the care of Dr. Brown-Séquard for some slight nervous disorder, I examined the urine and found it normal. I recognized sugar in the urine, March 22, 1878. Under a moderately strict diet the sugar promptly disappeared and was not discovered again until October 14, 1882, three years and nearly seven months after, although the diet was unrestricted during the greatest part of this time. This might have been regarded as a case of transient glycosuria if diabetes had not become confirmed in 1882 and 1883.

CASE XCII.—A gentleman, fifty-one years of age, 5 feet 11 inches tall, weighing 208 pounds. Five months before he came under my care he was examined for life insurance and no sugar was found in the urine. About three months later there were thirst, polyuria, weariness, etc., and sugar was found in the urine.

October 20, 1886.—The quantity of urine was 100 ounces containing 31 grains of sugar per ounce. The general diabetic symptoms were marked. The patient was put upon the antidiabetic diet and Clemens' solution. On October 27 the quantity of urine was reduced to 40 ounces and it contained no sugar. The diabetic symptoms had entirely disappeared. November 4 and 27 the conditions were the same. The patient then removed to the West. On January 28, 1887 he wrote me that he was perfectly well. On April 28 he wrote that he was as "good as new." Since his removal to the West the urine has been repeatedly examined and no sugar has been found. The treatment has been continued, with slight relaxation in the diet.

CASE LXXVII.—A gentleman, twenty-four years of age, 5 feet 5½ inches tall, weighing 132 pounds.

October 28, 1885.—The general diabetic symptoms were marked. The patient had lost twelve pounds in weight within the past three weeks. The quantity of urine was 112 ounces containing 28 grains of sugar per ounce. The patient was put upon the treatment already described. On January 6, 1886 the diabetic symptoms had disappeared and the quantity of urine was reduced to 50 ounces containing 4 grains of sugar per ounce. On May 19 and June 30 the urine contained no sugar. On September 8 the quantity of urine was 90 ounces containing 11½ grains of sugar per ounce. The diet had been imperfect for about two months.

March 2, 1887.—The urine was normal in quantity and it contained 9 grains of sugar per ounce. The patient had been eating freely of antidiabetic bread, which, as I have stated, probably contained about thirty per cent. of starch.

CASE LVIII.—A gentleman, forty-three years of age, 5 feet 9 inches tall, weighing 204 pounds. The disease is probably of eight or ten years' standing, but sugar was recognized in the urine only one year before the patient came under my care.

November 30, 1884.—The diabetic symptoms were marked. The urine was very abundant and contained 6 grains of sugar per ounce. The patient was put upon the treatment already described. On December 13 the symptoms had disappeared, the urine was reduced to the normal daily quantity and there was no sugar.

July 7, 1885.—The patient had been perfectly well. The urine had been examined seven times since December 13, 1884 and no sugar was found. The diet had been well carried out.

September 20, 1886.—The quantity of urine was 55 ounces. The morning urine contained 15½ grains of sugar per ounce and the evening urine, 30 grains. The diabetic symptoms had returned in a moderate degree.

October 12.—The urine was normal in quantity and contained 14½ grains of sugar per ounce. The antidiabetic treatment was

resumed. The diet had been unrestricted since October, 1885, the patient then regarding himself as cured.

October 16.—The urine was normal in quantity and contained $9\frac{1}{2}$ grains of sugar per ounce.

November 16.—The urine contained no sugar and the diabetic symptoms had disappeared. On January 24, 1887 the conditions were the same.

April 13, 1887.—The urine contained $1\frac{1}{2}$ grain of sugar per ounce. The patient had been travelling and the conditions for maintaining an antidiabetic diet were unfavorable. The patient had been eating freely of antidiabetic bread.

The ten cases reported are all that are now under my immediate observation. At the risk of being tedious, I have given certain details regarding these cases, although my records have been considerably abridged in this article. These cases seem to me to be quite instructive. Taken in connection with my other recorded cases, they lead me to the following conclusions:

I. In the three severe cases in which I have used the solution of lithium carbonate and sodium arsenate in carbonic acid water, no marked effects have been observed in the few weeks during which the remedy has been employed; but the treatment seems to me to be worthy of more extended trial and it may be useful in mitigating the severity of a strict antidiabetic diet.

II. The so-called specifics for diabetes have little if any effect. An exception, however, may be made in favor of the bromide of arsenic, which has sometimes seemed to me to control to a slight extent the thirst, polyuria and discharge of sugar.

III. The main reliance in treatment is to be placed upon an antidiabetic diet. This has fallen somewhat into disrepute because it is seldom efficiently carried out. In no single instance, out of ninety-nine recorded cases, have I found that the antidiabetic diet had been enforced.

IV. Milk should be absolutely interdicted. Its influence over the progress of the disease is prompt, powerful and most injurious.

V. There are certain cases in which dietetic treatment promptly arrests the glycosuria and keeps it under control. There are other cases in which treatment seems to be of little avail, except, possibly, in retarding the progress toward a fatal result. Of the ten cases reported and

now under observation, seven are amenable to treatment and three are obstinate.

VI. A confirmed diabetic may be cured, in the sense that all symptoms will disappear; but the disease is likely to return at any time under an unrestricted diet. Still, moderate care in diet will sometimes secure immunity.

VII. A patient who has once had diabetes should have his urine examined every few weeks. Glycosuria always precedes the general symptoms of the disease, and these general symptoms may sometimes be forestalled by proper treatment employed so soon as sugar makes its appearance in the urine.

VIII. As the disease returns, either from imprudences in diet or from other causes, the successive recurrences present greater and greater difficulties in the way of treatment.

XVIII

THE INFLUENCE OF EXCESSIVE AND PROLONGED MUSCULAR EXERCISE ON THE ELIMINATION OF EFFETE MATTERS BY THE KIDNEYS

Published in the "New York Medical Journal" for October, 1870.

IN the month of May, 1870, Weston, the pedestrian, attempted to walk one hundred miles in twenty-two consecutive hours. This feat was to be accomplished in an enclosure known as the Empire Skating Rink; a square building, well ventilated, in which a rectangular track was laid out, measuring nearly one-eighth of a mile. The weather was mild and clear, a pleasant day for that season of the year. This feat of endurance was accomplished in twenty-one hours and thirty-nine minutes. Attracted by the interest felt in this effort, I was present during the last three hours of the walk. It is not pertinent to the scientific questions involved to discuss the objections raised in regard to the exact measurement of the course, the style of walking, etc.; suffice it to say that, practically, Weston made one hundred miles, a few feet more or less perhaps, in twenty-two consecutive hours—a fact which none interested upon one side or the other have denied. While at the rink, I ascertained from the superintendent and judges that all of the urine passed during the walk had been collected, as a mere matter of convenience, in a single vessel. This urine I obtained entire and subjected it to analysis.

It is evident to any physiologist that there is much scientific interest attached to the quantitative analysis of the urine passed during such an expenditure of muscular and nervous force as is involved in walking one hundred miles in twenty-two hours; particularly in view of the recent observations of Fick and Wislicenus, Frankland, Haughton

and others, which seem to show that muscular exertion, under certain conditions of diet, does not increase the elimination of urea. This effort is nearly the maximum of what a person endowed with unusual powers of endurance is capable; and I embraced the opportunity of ascertaining what effect such an amount of muscular exercise would have upon disassimilation. To give full value to my observations, it became necessary to compare the elimination of effete matter during the walk with the daily excretion under ordinary conditions. In all points connected with these investigations, I have had the coöperation of Weston; but his absence from the city prevented my procuring a specimen of the ordinary urine until August. The specimen then obtained, however, seemed to me to answer perfectly for purposes of comparison.

Prefacing my observations with the statement that the idea of entering upon them originated during the last two hours of the walk, so that the comparison of the urine under exercise with the ordinary urine was necessarily made with a specimen collected some time after, I shall proceed to detail the facts observed and to make from them such physiological deductions as seem to be admissible. All the statements in regard to the condition, diet, etc., have been submitted to Weston and been carefully corrected.

Weston is thirty-one years of age, of medium height and rather lightly built, weighing, in ordinary clothing, about one hundred and thirty pounds. Allowing eight pounds for clothing, his ordinary weight would be about one hundred and twenty-two pounds. As would be expected of a person of such endurance his general health is perfect. His habits, as regards eating and sleeping, are very irregular. He is likely to be at work all night, sleeping part of the day, and his meals may be taken at any hour. He has never been through a regular system of training as a preparation for any of his pedestrian feats, but simply takes moderate exercise by walking. The following was his condition at the time of the walk:

The weight was one hundred and seventeen pounds, naked, allowing eight pounds for clothing. This is five pounds less than his ordinary weight. His physical condition was perfect. The lower limbs were well developed

and "fine," with the chest and upper extremities very light.

At 12.15 A. M., the walk was begun and the hundred miles were accomplished in twenty-one hours and thirty-nine minutes, ending at 9.45 P. M. At the end of the walk Weston did not seem fatigued, but appeared brisk and bright and was as well as ever on the following day. No urine was passed up to 10.15 P. M.; so that the urine collected was practically the urine of twenty-two hours.

During the walk Weston took the following articles of food in small quantities and at short intervals:

Between one and two bottles of beef-essence; two bottles of oatmeal-gruel; sixteen to eighteen eggs, raw, in water. He drank a little lemonade and took water very frequently, a mouthful at a time, only to rinse his mouth. While walking the last ten miles he took two or three swallows of champagne and about two and a half fluidounces of brandy in ten-drop doses. The head and face were sponged freely at short intervals and the food and drink were taken mainly on the walk.

All the urine that was passed during the walk was received into a pail in a little muslin enclosure by the side of the track. There was no discharge from the bowels during that time. I have taken the quantity as representing twenty-two hours; and have calculated from that the quantity to represent twenty-four hours.

All the analyses were made by the processes described in my little work on "Chemical Examination of the Urine." The urea was estimated by Davy's method with hypochlorite of soda, the French Labarraque's solution, a solution which had been carefully corrected and compared with Liebig's method. The chlorine was estimated by a graduated solution of nitrate of silver; the sulphuric acid, by a graduated solution of chloride of barium; and the phosphoric acid, by a graduated solution of sesquichloride of iron. The uric acid was estimated by actual weight, evaporating the urine to a thick syrup, extracting the urea, creatin, creatinin and coloring matter with absolute alcohol, setting free the uric acid and extracting the inorganic salts with very dilute hydrochloric acid, and collecting the uric acid on a filter. The processes in the analyses of both specimens of urine were identical. The examination was

begun about fourteen hours after the last urine had been passed. The examination of the specimen taken for comparison was begun sixteen hours after it had been collected.

EXAMINATION OF URINE PASSED DURING THE WALK

Weight of body, without clothing, one hundred and seventeen pounds.

Articles of food and drink taken: Beef-essence, between one and two bottles; oatmeal-gruel, two bottles; sixteen to eighteen eggs, raw, in water; lemonade, about half a pint; champagne, about three fluidounces; brandy, two and a half fluidounces; water to rinse the mouth every few minutes, and but little swallowed.

No sleep during the twenty-two hours.

TABLE I.—COMPOSITION OF THE URINE

Quantity in the twenty-two hours, 73½ fluidounces (estimated for twenty-four hours, 80 fluidounces); acidity normal; color rather light canary; odor strongly urinous but normal; specific gravity, 1011.55; no abnormal matters; microscopical examination negative.

	Per fluidounce.	In 22 hours.	Per hour.	In 24 hours.
Urea	5.779 grains.	424.756 grains.	19.307 grains.	463.368 grains.
Chlorin	1.120 "	82.320 "	3.742 "	89.808 "
Sulphuric acid.....	0.920 "	67.620 "	3.074 "	73.776 "
Phosphoric acid (total)	1.504 "	110.544 "	5.025 "	120.600 "
Phosphoric acid (with alkalis) *	1.280 "	94.060 "	4.275 "	102.600 "
Phosphoric acid (with earths) *	0.224 "	16.484 "	0.750 "	18.000 "
Uric acid	0.500 "	36.750 "	1.670 "	40.080 "

On August 20, 1870 Weston began to collect for me the urine of the twenty-four hours, from 6 P. M., the 20th, to 6 P. M., the 21st. The weather was warm but not oppressive. His habits of life were about the same as before his walk of May 25. He wrote the greater part of the night of the 19th and slept from 4.30 A. M. to 8.15 A. M. of the 20th.

* Approximative.

He then went up the Hudson River, and on the steamboat took a light breakfast at 11 A. M., consisting of rare beef-steak, fried potatoes and cold bread with water. Between that time and 3 P. M. he walked two miles. At 3 P. M. he took dinner as follows: Broiled ham with eggs, stewed tomatoes, fried potatoes and sweet corn, drinking one glass of fresh milk and two glasses of claret wine with water. At 5.45 he ate of muskmelon and a few pears.

He began to collect the urine at 6 P. M. At 7 P. M. he ate a supper of pickled lambs' tongues with warm, light biscuit and drank one cup of tea. He slept from midnight till 7 A. M., then rose for a moment, retiring again and sleeping until 12 M. of the 21st. At 2 P. M. he ate a hearty breakfast (or dinner) of cold corned beef, hot bread-cakes and one slice of bread and drank one cup of coffee. He did not eat again until after 6 P. M., the limit of the time for collecting the urine.

During the afternoon of the 21st he drank one glass of Ottawa beer (a mild, effervescing root-beer) and smoked two cigars.

At 11 P. M. August 20 he had an evacuation of the bowels but did not lose any urine.

EXAMINATION OF THE URINE OF TWENTY-FOUR HOURS UNDER ORDINARY CONDITIONS

Weight of body without clothing, one hundred and twenty-two pounds.

Articles of food and drink taken: Supper—Pickled lambs' tongues, warm, light biscuit, one cup of tea. Dinner—Cold corned beef, hot bread-cakes, one slice of bread, one cup of coffee. One glass of Ottawa beer and two cigars during the day.

Slept between eleven and twelve hours. Ate salt ham the day before at 3 P. M.

TABLE II.—COMPOSITION OF THE URINE

Quantity in twenty-four hours, 33 fluidounces; acidity rather faint; color rather light canary and slightly turbid; odor strongly urinous but normal; specific gravity 1025.43; no abnormal matters; decomposed rather rapidly; micro-

scopical examination showed a rather untusual quantity of mucus, otherwise negative.

	Per fluidounce.	Per hour.	In 24 hours.
Urea.....	5.800 grains.	7.975 grains.	191.400 grains.
Chlorin.....	3.360 "	4.620 "	110.880 "
Sulphuric acid.....	1.440 "	1.980 "	47.520 "
Phosphoric acid (total).....	0.960 "	1.320 "	31.680 "
Phosphoric acid (with alkalis)*....	0.640 "	0.880 "	21.120 "
Phosphoric acid (with earths)*....	0.320 "	0.440 "	10.560 "
Uric acid.....	0.680 "	0.935 "	22.440 "

TABLE III.—COMPARISON OF THE URINE PASSED UNDER ORDINARY CONDITIONS (REST) WITH THE URINE PASSED DURING THE WALK OF ONE HUNDRED MILES IN TWENTY-TWO HOURS (EXERCISE)

	PER HOUR.		IN TWENTY-FOUR HOURS.		
	Rest.	Exercise.	Rest.	Exercise.	Percentage of difference.
Total quantity..	1.375 oz.	3.341 oz.	33.000 oz.	80.000 oz.	142.424 increase.
Urea.....	7.975 grs.	19.307 grs.	191.400 grs.	463.368 grs.	142.094 "
Chlorin.....	4.620 "	3.742 "	110.880 "	89.808 "	19.004 decrease.
Sulphuric acid..	1.980 "	3.074 "	47.520 "	73.776 "	55.252 increase.
Phosphoric acid (total).....	1.320 "	5.025 "	31.680 "	120.600 "	280.681 "
Phosphoric acid (with alkalis).	0.880 "	4.275 "	21.120 "	102.600 "	365.800 "
Phosphoric acid (with earths)..	0.440 "	0.750 "	10.560 "	18.000 "	70.454 "
Uric acid.....	0.935 "	1.670 "	22.440 "	40.080 "	78.609 "

The foregoing tables show the effects of prolonged muscular exercise upon the general process of disassimilation, as indicated by the elimination of effete matters by the kidneys; and this is all the more marked as the exertion probably reached to near the limit of endurance. By reference to Table III. it will be seen that the variations under repose and exercise are very great. It was impossible to compare two specimens of the urine of the twenty-four hours taken under conditions of diet precisely identical, which would have made the observations upon the effects of muscular exercise much more satisfactory; but physiologists are now sufficiently familiar with the effects

* Approximative.

of diet upon the composition of the urine to enable them to separate these influences and appreciate the modifications produced by the great strain upon the muscular system. I shall proceed, therefore, to consider these changes, taking into account the disturbing influences of the variations in the food and drink.

TOTAL QUANTITY OF URINE.—The quantity of water in the urine was much greater during exercise, the excess over the quantity passed under ordinary conditions amounting to nearly one hundred and fifty per cent. This I attribute in a measure to the excessive muscular exertion and in part to the large quantity of liquids taken and the fact that the skin did not act very freely. It is a fact that an increase in the water of the urine, even when due entirely to the ingestion of liquids, increases the absolute quantity of solid matters excreted.

UREA.—The most interesting point in connection with these investigations relates to the excretion of urea; and in considering this it will be necessary to consider the influence of diet. By reference to Table II., which gives the composition of the urine under ordinary conditions, it will be seen that the proportion of urea is smaller than one would expect, judging from the specific gravity, but that the chlorides are largely in excess. The total quantity in the twenty-four hours is very small, hardly two hundred grains. On inquiry, I ascertained that Weston is a small eater; and on that day he ate but twice, slept twelve hours and took very little exercise. His diet, also, on that day contained but little nitrogenous matter. These facts taken in connection with his weight, which was but one hundred and twenty-two pounds, in part account for the small quantity of urea.

On the day of the walk the elimination of urea was enormous in proportion to the weight of the body, amounting to four hundred and sixty-three grains, nearly one and a half times more than on the day of repose. The question here arises as to how far this is due to conditions of diet, and what proportionate increase is to be attributed to the great muscular exertion:

I. The excess of water eliminated by the kidneys would account for a small part, but only a small part, of the increase of urea.

II. The diet on the day of the walk contained a large amount of nitrogenous matter; among other articles, sixteen to eighteen raw eggs. This will account for a considerable proportion of the excess of urea; and it remains to see how much can reasonably be referred to this source.

III. The most complete series of observations upon the effects of nitrogenous food on the elimination of urea are those of Lehmann.* In these observations, made on his own person, Lehmann found that he excreted, on a well-regulated mixed diet, 501.6 grains of urea in twenty-four hours. On a purely animal diet, taking, as one item, thirty-two eggs, he excreted 821 grains, an excess of nearly sixty-four per cent. In the case of Weston, who took about half the number of eggs, there was an excess of one hundred and forty-two per cent., leaving an excess, due to his long-continued exertion, of seventy-eight per cent. Lehmann also found that while he took in the eggs 465.5 grains of nitrogen, he discharged only 387.8 grains of nitrogen in the urea.

I do not propose to discuss critically the many observations that have been made within the last few years on the influence of muscular exercise, conjoined with peculiar diet, upon the elimination of urea. So far as I know, on no occasion has this point been investigated when the muscular exertion has been so severe and prolonged. There can be hardly any doubt that in the case of Weston the feat of endurance which he accomplished increased the elimination of urea by seventy-five or a hundred per cent.

CHLORIDES.—During the walk the chlorides in the urine seemed to be below the average, while they were in excess for the day of repose. The influence of the exercise on the proportion of chlorides does not seem to be very marked. On the day when the normal urine was taken, the diet included a considerable quantity of salt in the corned beef, and on the day before, salt ham was taken at 3 P. M., three hours before the urine was collected. The variations in the chlorides may possibly be accounted for by the diet.

SULPHATES AND PHOSPHATES.—The total quantity of sulphates was considerably increased during the day of the

* Lehmann, "Physiological Chemistry," Philadelphia, 1855, vol. i., p. 150 *et seq.*

walk. This is in accordance with all observations on this point.

The proportion of phosphates on the day of the walk was nearly quadrupled. This is a very interesting fact, as the phosphates constitute a large and essential part of the inorganic constituents of the tissues. A part of the great excess was probably due to the muscular exertion and want of sleep, and a part to the large preponderance of animal food.

URIC ACID.—The muscular exertion increased, by about seventy-eight per cent., the elimination of uric acid; but the proportion per fluidounce was less during the exercise than in repose. The theory has been advanced that exercise increases urea and diminishes uric acid, the latter undergoing oxidation more rapidly. My observations are not conclusive on this point. The diminution in the proportion of uric acid per fluidounce would seem to show that oxidation was more rapid under exercise, the immense increase in urea being also an argument in favor of this view.

In conclusion, these observations seem to show that excessively severe and prolonged muscular exercise increases largely the quantity of nitrogenous excrementitious matters eliminated in the urine, particularly urea, and produces a corresponding increase in the elimination of most of the inorganic salts.

XIX

ON THE EFFECTS OF SEVERE AND PROTRACTED MUSCULAR EXERCISE ; WITH SPECIAL REFERENCE TO ITS INFLUENCE ON THE EXCRETION OF NITROGEN

Published in the "New York Medical Journal" for June, 1871.

PART I

IN May, 1870 I had an opportunity of examining the entire urine passed by Weston, the pedestrian, during the time occupied in accomplishing the feat of walking one hundred miles in twenty-one hours and thirty-nine minutes. The urine on that occasion happened to have been passed into a single vessel and had been undisturbed until it came into my possession. I had no means of obtaining any reliable scientific information in regard to the quantity and character of the food taken during that time, nor had I obtained, for purposes of comparison, a specimen of the urine passed on the day before this muscular effort. It was several weeks, indeed, before I could get the urine of twenty-four hours of comparative repose; which I was forced to take as representing the normal excretion. I simply took the material for scientific analysis as I could best obtain it and published the results with a statement of the facts, not at that time entertaining any definite hope of being able to repeat the investigations under more favorable conditions. I was, of course, well aware of the necessity of carefully estimating certain constituents of the food, and of comparing the elimination of effete matters, particularly those containing nitrogen, with the matters ingested. Had I been sure of an opportunity to study the effects upon excretion of excessive and prolonged muscular exercise, such as has since presented itself, my first

experiments, of the unavoidable defects of which no one could be more sensible than I, would not have been published. My first observations have been excluded in the present inquiry on account of the imperfect data on which they were based; but I may anticipate my conclusions from these more complete experiments far enough to state that the results have been essentially the same.

In the summer of 1870 Weston proposed to make an attempt to walk four hundred miles in five consecutive days and upon one of those days to walk one hundred and twelve miles in twenty-four consecutive hours. He offered to submit himself to any scientific observations that I might wish to undertake in connection with this effort. This offer was accepted; and I have endeavored to make this occasion to the fullest extent useful to physiological science. The investigations to be made seemed to me of such importance, particularly in the present unsettled state of opinion upon some points connected with nutrition and disassimilation, that I asked the aid of certain well-known scientists, in formulating and carrying out a series of experiments which should be as complete as possible.

The following gentlemen consented to lend to the proposed work the advantage of their scientific experience and judgment: Dr. R. Ogden Doremus, Professor of Chemistry in the Bellevue Hospital Medical College and in the College of the City of New York; Dr. J. C. Dalton, Professor of Physiology in the College of Physicians and Surgeons; and Dr. W. H. Van Buren, Professor of the Principles of Surgery, etc., Dr. Austin Flint, Professor of the Principles and Practice of Medicine, and Dr. Alexander B. Mott, Professor of Surgical Anatomy, all of the Bellevue Hospital Medical College.

At a meeting held some weeks before the walk a definite plan of investigations was agreed upon. Prof. Doremus assumed the responsibility of all of the necessary chemical analyses, and I proposed to take charge myself of the remaining scientific work and to superintend the records of diet, etc. The plan of operations agreed upon will be fully detailed farther on, as an introduction to an account of our observations; but this may be anticipated at the outset by a few general statements.

It was proposed to make our observations for three

distinct periods; viz., first period, five days before the walk; second period, the five days of the walk; third period, five days after the walk. For the fifteen days during which Weston was to be under observation, it was proposed to have a trusty assistant with him every instant, day and night, who was to weigh his food and drink and make notes under the direction of one of our number. This was done by Mr. Thomas C. Doremus, Jr., who performed his task in the most faithful and accurate manner. The urine and feces were sent to the laboratory of Prof. Doremus, where they were analyzed under his direction by his assistant, Mr. Oscar Loew. The necessary analyses of food were also made by Mr. Loew.

The material thus collected, with a complete record of the walk, finally passed into my hands for classification and analysis. Before this report was written, the tables of food, composition of urine, feces, etc., were calculated. This alone has been a labor of several weeks, and no pains has been spared to secure entire accuracy. The numerical calculations were all made by two or more different methods, so that it has seemed almost impossible that any error of importance should have been overlooked. Taking, as I have, the bare records and analyses made by Mr. Doremus and Mr. Loew, with entire ignorance of their probable results, the calculations proceeded steadily to their mathematical conclusions, which were apparent only at the time of their actual completion.

In the preparation of this paper I have attempted to present the scientific data in such a form as to be easily available as ascertained facts, to any who may not admit the interpretation I have put upon them.

It may serve to make the bearing of our observations more easily comprehended to give a succinct statement of the generally-received physiological views regarding certain of the points involved. In this I do not propose to analyze the literature of the subject, even for the past few years; and I desire especially to avoid controversial discussion. I do not intend to criticise the experiments of others or to point out their defects, except in so far as these defects may seem to be supplied by my more extended opportunities for investigations in particular directions.

VIEWS OF PHYSIOLOGISTS IN REGARD TO THE INFLUENCES OF EXERCISE, DIET, ETC., UPON THE ELIMINATION OF NITROGENOUS EXCREMENTITIOUS MATTERS, CHIEFLY UREA

Following the researches of Lavoisier on the chemical phenomena of respiration and their relations to animal heat, the theories of Liebig, who divided the food into two classes, plastic and calorific, were almost universally accepted by physiologists. Liebig advanced the view that the articles of food composed of carbon, hydrogen and oxygen, were chiefly if not entirely useful in maintaining the animal temperature, by entering into combination with the oxygen of the inspired air, producing carbonic acid, water and heat. He regarded the food composed of carbon, hydrogen, oxygen and nitrogen as concerned chiefly, if not entirely, in repairing the waste of the nitrogenous parts of the living body, particularly the muscular tissue. Applying these views to muscular action, Liebig assumed that exercise was always attended with an increased activity in the destructive metamorphosis of the nitrogenous substance of the muscular tissue; and that this could be measured by the quantity of urea excreted. The following is a quotation from one of his earlier works:

"Boiled and roasted flesh is converted at once into blood; while the uric acid and urea are derived from the metamorphosed tissues. The quantity of these products increases with the rapidity of transformation in a given time, but bears no proportion to the amount of food taken in the same period. In a starving man, who is any way compelled to undergo severe and continued exertion, more urea is secreted than in the most highly-fed individual if in a state of rest."*

Again, Liebig makes the general statement that "the amount of tissue-metamorphosis in a given time may be measured by the quantity of nitrogen in the urine."†

For many years this view of the source of the nitrogenous excrementitious matters and the laws which regulate the activity of their production was received by physiologists almost without question. It was modified, however, a few years later by the researches of Lehmann; who showed by a large number of observations on his own

* Liebig, "Animal Chemistry, or Chemistry in its Applications to Physiology and Pathology," London, 1843, p. 138.

† *Ibid.*, p. 245.

person that, other conditions being equal, the character and quantity of food modified very greatly the elimination of urea, as is seen in the following quotation:

"My experiments show that the amount of urea which is excreted is extremely dependent on the nature of the food which has been previously taken. On a purely animal diet, or on food very rich in nitrogen, there were often two-fifths more urea excreted than on a mixed diet; while, on a mixed diet, there was almost one-third more than on a purely vegetable diet; while, finally, on a non-nitrogenous diet, the amount of urea was less than half the quantity excreted during an ordinary mixed diet."*

Lehmann further states, however, that upon a uniform diet the elimination of urea is increased by muscular exercise.

The views of Liebig, modified by the researches of Lehmann, were pretty generally accepted up to 1866; notwithstanding that Bischoff had advanced experiments to show that the elimination of nitrogen by the kidneys was regulated almost entirely by the quantity of nitrogen in the ingesta.†

In 1866 Fick and Wislicenus published an account of experiments made in ascending one of the Alpine peaks, the Faulhorn, about 6,500 feet high. These experiments were undertaken with the view of showing that severe and prolonged muscular effort could be accomplished upon a non-nitrogenous diet. The two experimenters took no proteid food from midday on August 29 until 7 P. M. of August 30. The experiments proper began on the evening of the 29th, at a quarter past 6 P. M., with a complete evacuation of the bladder. The urine from this time till ten minutes past five on the morning of the 30th (about eleven hours) was collected and called the "night-urine." The ascent began at ten minutes past five and occupied eight hours and ten minutes. The urine passed during this period was collected as "work-urine." The urine for five hours and forty minutes after the ascent was collected as "after-work urine." The urine from 7 P. M., August 30 till half-past five A. M., August 31 was

* Lehmann, "Physiological Chemistry," Philadelphia, 1855, vol. i., p. 150.

† Bischoff, "Der Harnstoff als Maas des Stoffwechsels," Giessen, 1853. In 1860 these researches were considerably extended by Bischoff and Voit. Bischoff und Voit, "Die Gesetze der Ernährung des Fleischfressers," Leipzig und Heidelberg, 1860.

collected and designated as "night-urine." The results of the examinations of these specimens in the two persons were nearly identical. The following is the estimate of the elimination of nitrogen per hour during the different periods: *

	Fick.	Wislicenus.
During the night, 29th to 30th..	0.63 grammes.	0.61 grammes.
During the time of work.....	0.41 "	0.39 "
During rest after work.....	0.40 "	0.40 "
During the night, 30th to 31st..	0.45 "	0.51 "

From these results Fick and Wislicenus conclude that muscular exercise does not necessarily increase the elimination of nitrogen; that the substance of the muscle itself is consumed in insignificant quantity; and that the muscular system is a machine, consuming in its work, not its own substance, but fuel, which is supplied by the food. The most efficient fuel Fick and Wislicenus consider to be non-nitrogenous food; the results of its consumption being force, or work, heat and carbonic acid. They adopt the view "that the substances, by the burning of which force is generated in the muscles, are not the albuminous constituents of the tissues, but non-nitrogenous substances, either as fats or hydrates of carbon."

"We might express this doctrine by the following simile: A bundle of muscle-fibres is a kind of machine consisting of albuminous material, just as a steam-engine is made of steel, iron, brass, etc. Now, as in the steam-engine coal is burnt in order to produce force, so, in the muscular machine, fats or hydrates of carbon are burnt for the same purpose. And in the same manner as the constructive material of the steam-engine (iron, etc.) is worn away and oxidized, the constructive material of the muscle is worn away, and this wearing away is the source of the nitrogenous constituents of the urine. This theory explains why, during muscular exertion, the excretion of the nitrogenous constituents of the urine is little or not all increased, while that of the carbonic acid is enormously augmented; for, in a steam-engine, moderately fired and ready for use, the oxidation of iron, etc., would go on tolerably equably, and would not be much increased by the more rapid firing necessary for working, but much more coal would be burnt when it was at work than when it was standing idle."†

I have made these quotations from the paper of Fick and Wislicenus for the reason that the theories advanced

* Fick and Wislicenus, "On the Origin of Muscular Power."—"London, Edinburgh and Dublin Philosophical Magazine," London, January-June, 1866, vol. xxxi., p. 492.

† *Loc. cit.*, p. 501.

and the experiments reported have changed very materially the current of physiological opinion in regard to the origin of muscular force and the significance of the elimination of nitrogen. The question is not materially modified or advanced by the papers of Frankland * or of Haughton,† who sustain fully the views of Fick and Wislicenus, which are now adopted very largely, particularly in Germany and England.

The opposite view, that the elimination of nitrogen is to a great extent a measure of the waste of the nitrogenous constituents of the tissues and that this is increased by exercise, is substantially the one advanced by Liebig. Almost all observers who have experimented on the influence of exercise upon the elimination of urea, under an ordinary diet, have found its excretion markedly increased. In 1867 experiments were made by Parkes upon two soldiers, with the view of controlling the experiments of Fick and Wislicenus by observations upon a more extended scale.‡ These experiments failed to confirm those of Fick and Wislicenus. They were continued for a period of eighteen days and certainly seemed to show an increase in the urea, attributable to muscular exercise. The extraordinary exercise taken was a walk of 23.70 miles on one day and 32.78 miles on the day following. During these two days, on an exclusively non-nitrogenous diet, the elimination of nitrogen was slightly increased over a period of two days of rest and non-nitrogenous diet. In an analysis of a recent course of lectures delivered by Dr. Parkes at the College of Physicians, London, it appears that he is disposed to take a view of the subject between the two extremes; viz., that the muscular system is able to accomplish work by the consumption of non-nitrogenous food; that exercise does, however, slightly increase the elimination of urea and that during exercise a small portion of the muscular substance is consumed; but he is of the opinion that the variations

* Frankland, "On the Origin of Muscular Power."—"London, Edinburgh and Dublin Philosophical Magazine," London, July-December, 1866, vol. xxxii. p. 182, *et seq.*

† Haughton, "Address on the Relation of Food to Work done by the Body, and its Bearing upon Medical Practice."—"The Lancet," London, August 15, August 22, and August 29, 1868.

‡ Parkes, "On the Elimination of Nitrogen by the Kidneys and Intestines, during Rest and Exercise, on a Diet without Nitrogen."—"Proceedings of the Royal Society," London, 1867, vol. xv., No. 89, p. 339 *et seq.*

in the quantity of nitrogen eliminated are almost entirely dependent upon the quantity of nitrogen contained in the food.*

One desirous of consulting further the literature of this question may find, in a recent article by Liebig, a full discussion of the subject of the source of muscular power from his own point of view.† He analyzes very fully the experiments of Parkes, and he finds in the results fresh testimony in favor of his view that the increase in the elimination of nitrogen as a consequence of muscular exercise is not limited to the period of exertion but continues for some time after. On the other hand, Voit has lately published an elaborate paper reviewing the publications on this question that have appeared during the last twenty-five years.‡ Neither of these papers adds to the sum of physiological knowledge by the contribution of new experimental facts; but they are interesting as expressing the arguments upon two opposite sides, and they illustrate the necessity of new observations, in which some of the important omissions in the experiments hitherto made may be supplied.

PLAN OF THE INVESTIGATIONS AND THE PROCESSES EMPLOYED

A few weeks before Weston put himself under our observation, he was made to undergo a thorough physical examination at the hands of Prof. Austin Flint, and his urine was examined by myself. The result showed that Weston was in perfect health, at least so far as could be determined by any ordinary physical examination. This examination was made in order to ascertain whether or not there existed any physical reason why it would be unsafe for Weston to undertake his proposed task.

Having ascertained that Weston was in perfect health, he was invited to be present at a meeting for the purpose of fixing upon a definite plan of investigation. At this meeting were present, Profs. Doremus, Dalton, Van Buren,

* "Abstract of the Croonian Lectures delivered at the College of Physicians by Dr. Parkes."—"Medical Times and Gazette," London, March 15, 1871, p. 348.

† Liebig, "The Source of Muscular Power."—"The Pharmaceutical Journal and Transactions," London, 1870, Third Series, part ii., p. 161, and part iii., pp. 181, 201, 221.

‡ Voit, "Ueber die Entwicklung der Lehre von der Quelle der Muskelkraft und einiger Theile der Ernährung seit 25 Jahren."—"Zeitschrift für Biologie," München, 1870, Bd. vi., S. 305 *et seq.*

Flint and myself. Weston was here subjected to another examination with reference to his physical condition, which was found to be perfect.

As the result of our deliberations at this meeting it was decided to confine our investigations within limits that would render it possible to complete them accurately and satisfactorily; the fear being that in attempting to do too much the value of our results might be impaired. It was also deemed proper to take the position that we would under no circumstances interfere with Weston's diet, training or manner of making the walk, simply observing the facts according to our plan. This was fully carried out. Throughout the entire fifteen days during which Weston was under observation, he acted in everything according to his own judgment; and the walk was made without any advice or interference on the part of any of those engaged in the investigations.

In collecting our material it was determined to note the following points:

I. To take our observations during three periods; viz., a first period, five days before the walk; a second, the five days of the walk; and a third, five days after the walk. Inasmuch as we proposed to assume the entire responsibility of the accuracy of all the facts noted, it was determined to place Weston in the hands of Mr. Thomas C. Doremus, Jr., son of Prof. Doremus, who was not to leave him, night or day, without notifying the person in charge of the investigations. Mr. Doremus was actually with Weston, night and day, for the fifteen days, except on two occasions. On one day, for a few hours, Mr. Doremus' place was supplied by Mr. Loew, assistant to Prof. Doremus, who was engaged in making the chemical analyses. On another occasion, Mr. Doremus was relieved by me for about four hours. During the walk, Prof. Mott, Prof. Doremus and I, one or all of us, were constantly present at the rink. Mr. Doremus was with Weston almost constantly at this time, but he occasionally slept in the building, when Weston was walking at night, leaving him in charge of one of us. It is necessary to make these statements, in view of the extraordinary character of our results, to show that nothing is taken as a fact to work upon unless observed by ourselves or our assistants.

II. To take every day, as nearly as possible at the same hour and under the same conditions, the naked weight, pulse, respirations and temperature.

III. To note accurately the weight of every separate article taken as food or drink. This was done for two purposes: to note the ingesta and excreta, with reference to the weight of the body; and to have all the articles of food separately weighed, so as to estimate the daily consumption of nitrogen.

IV. To note the amount of exercise taken each day, in the first period, before the walk, and in the third period after the walk; and also to note anything unusual with reference to his general condition.

V. To collect the entire urine of the twenty-four hours, day by day, for the purpose of subjecting it to chemical and microscopical examination. As Weston proposed to arrange in his walk of five days that the time should expire a few minutes after midnight, the twenty-four hours for collecting the urine were calculated from midnight to midnight. It was also decided to collect and weigh the feces.

In the execution of the above plan I assumed the responsibility of superintending the records, except the notes of the chemical analyses, and of making microscopical examinations of the urinary sediments. Prof. Doremus assumed the responsibility of the chemical analyses. So far as the general records are concerned, I have no hesitation in testifying to their entire accuracy. It is fortunate that no accident happened, such as the breaking of a bottle or a glass, and the only error was in taking the weight on November 23, the third day of the walk. Prof. Doremus is equally satisfied in regard to the chemical analyses made by his assistant, Mr. Oscar Loew.

The details of the plan as it was carried out are as follows:

Mr. Doremus, Mr. Loew and I were each provided with a notebook. My own notebook was for recording the microscopical examinations of the urinary sediments.

The following directions were written in the notebook given to Mr. Doremus:

At every meal weigh the food and drink in the following manner:

Put the meat on a separate plate and weigh the plate

before and after eating. Note the loss of weight, which will give the quantity actually consumed. Weston does not intend to eat much fat, but expects to get his fat from butter. When he eats fat it is to be noted.

Put each vegetable on a separate plate and determine the quantity consumed, in the same way as for the meat.

Estimate the bread in the same way as the meat and vegetables.

Take a known weight of butter and weigh each night to ascertain the quantity taken during the day. It will be sufficient to determine in this way the quantity of butter consumed in the twenty-four hours.

Estimate the quantity of sugar taken, in the same way as for the butter.

Note the number of eggs taken and see that they are entirely consumed.

Measure the water taken, by fluidounces, and always carry a graduated glass for Weston to drink from, so that the quantity shall be taken exactly.

Measure the coffee, tea and any other liquids taken, in the same way, and note especially the quantity of milk used.

Each night, just before Weston goes to bed, take the weight of the body, naked, the temperature under the tongue, the pulse and respirations, and note the time when the above-mentioned conditions are observed. The pulse is always to be counted sitting. The respirations are to be taken in the same position, when Weston's attention is diverted and when he is perfectly tranquil.

Note the exercise, miles walked, time, etc., for each twenty-four hours.

Collect all the urine for each twenty-four hours. Send six fluidounces to me for microscopical examination and send the remainder to the chemical laboratory for quantitative analysis. Before any of the urine is sent, mix the whole for the twenty-four hours and note on the bottle sent to the chemical laboratory the quantity taken out for microscopical examination, so that the chemist may take this into account in his record of the entire quantity.

Collect the feces and send them each day to the chemical laboratory.

At the end of each record for the day, note the general

condition of health and feelings and any unusual circumstance that may have occurred during the day affecting the physiological conditions.

Note each fact instantly, leaving nothing to the memory. Read these directions carefully every night before closing the record for the day and supply at once any omissions.

The following directions were written in the notebook given to Mr. Loew:

Measure the entire quantity of urine in the twenty-four hours.

Note the odor, color, reaction and specific gravity.

Note the presence or absence of albumin or sugar.

Ascertain the proportions of various constituents of the urine, according to directions received from Prof. Doremus.

Be careful to note each day accurately from midnight to midnight.

The weight was taken each night, generally in my presence, by Mr. Doremus, as near midnight as practicable, upon new platform-scales, weighing accurately to a quarter of a pound. The food was weighed upon a new balance, weighing accurately to $\frac{1}{4}$ of an ounce. These balances were selected on account of their accuracy and their availability for rapid weighing, inasmuch as it was desirable to annoy Weston as little as possible, particularly in giving him his weighed food. The pulse, respirations and temperature were noted by me, except on the evening of November 16th, when they were noted by Prof. Dalton. The temperature was taken under the tongue with a maximum thermometer, graduated to $\frac{1}{10}$ of a degree Centigrade.

The weight of the food was taken in the manner indicated. The liquids were measured in a graduated glass, as a matter of convenience; but their weights were calculated in the final tables.

Having taken the weight of each article of food, it was desired to ascertain the quantity of nitrogen in the ingesta. After consulting the works at my command giving analyses of different articles of food, I compiled the following table from Payen. It was at first thought desirable to subject specimens of each article to analysis for nitrogen; but the conditions under which the observations were carried out seemed to render the estimates of Payen quite as useful.

It was assumed at the outset that we were not to interfere with the diet in any way, noting only the articles taken. Weston's food was taken at several different places and was prepared by different persons; and it would have been impossible to have analyzed actual specimens of each article. In view of this fact, it seemed probable that the variations from our analyses, should we have made them, would have been as considerable as the variations from the average estimates given by Payen. It has been ascertained, also, that the flesh of different animals presents but a small fraction of a percentage of difference in the nitrogen. All the meats, therefore, are classed together in the table and are assimilated to the composition of cooked beef, which contains about 3.5 per cent. of nitrogen.* No estimate could be found of the proportion of nitrogen in the beef-essence, head-cheese or oatmeal-gruel; and these articles were analyzed for nitrogen by Mr. Oscar Loew, by the ordinary method; viz., treating the dry residue after evaporation with soda-lime and determining the nitrogen as ammoniochloride of platinum, reducing the metallic platinum by heat. The estimates of the proportions of nitrogen in the food were therefore approximative; but the percentage that might properly be allowed for error would be very slight. Even if this should be taken at the almost impossible figure of ten per cent., it would not modify the results. The advantage of experimenting upon a normal and unrestricted diet seems to me to more than compensate for the necessarily approximative estimates of the quantities of nitrogen consumed.

PROPORTIONS OF NITROGEN PER HUNDRED PARTS

ARTICLE.	NITROGEN.	AUTHORITY.
Beef. . .	3.50	{ Payen, p. 488. This is the approximative estimate for cooked beef.
Mutton.		
Chicken		
Turkey.		
Fish . . .		
Eggs.....	1.90	Payen, p. 488.
Beef-essence	0.87	O. Loew (actual analysis).
Head-cheese	2.24	" "
Milk	0.66	Payen, p. 488.
Custard.....	1.28	Average of milk and eggs.

* Payen, "Précis théorique et pratique des substances alimentaires," Paris, 1865, p. 488 *et seq.*

ARTICLE.	NITROGEN.	AUTHORITY.
Ice-cream.....	1.28	Average of milk and eggs.
Cream-cakes.....	1.28	" "
Oysters.....	2.13	Payen, p. 489.
Cheese.....	4.12	" "
Bread (includes corn-cakes, cake, crackers and bread- pudding).....	1.08	Payen, p. 490.
Rice-pudding (rice and custard)	1.18	" " ; Rice, p. 180.
Oatmeal-gruel.....	0.086	O. Loew (actual analysis).
Potatoes.....	0.33	Payen, p. 490.
Figs.....	0.92	" "
Butter.....	0.64	" "
Coffee.....	0.11	" "
Tea.....	0.02	" "
Tomatoes.....	} These articles contain no nitrogen or merely a trace which may be disregarded.	
Cranberries.....		
Cauliflower.....		
Celery.....		
Lettuce.....		
Tomato-soup.....		
Tomato-catsup.....		
Grapes.....		
Apples.....		
Citron.....		
Preserves.....		
Sweet pickles.....		
Sugar.....		
Lemonade.....		
Molasses-and-water..		
Vinegar.....		
Salt.....		
Pepper.....		
Bicarbonate of potash		

The urine of each twenty-four hours was carefully collected in a large glass-stoppered bottle and was analyzed by Mr. Loew by the following methods:

The specific gravity was always determined by actual weight.

The urea was estimated by Liebig's volumetric process. In this, a single specimen of urine was used for estimating both chloride of sodium and urea. The chloride of sodium was determined first, and afterward the urea was determined with a different mercurial solution. This was done to avoid confusion and possible mistakes in the readings of the burettes.

The uric acid was determined by weight; concentrating the urine, treating it for twelve hours with nitric acid, and collecting the crystals of uric acid.

The phosphoric acid was determined by weight, converting the phosphates into $M_6HPO_4 + 7H_2O$.

The sulphuric acid was determined by weight, converting the sulphates into $BaSO_4$.

The examination of the urinary sediments was made by myself with a $\frac{1}{4}$ inch objective, allowing the specimen to stand for about twelve hours.

The feces were passed directly into clean glass vessels provided with air-tight glass covers, and weighed. The nitrogen of the feces was estimated by the soda-lime and platinum process.

PHYSIOLOGICAL HISTORY OF WESTON FOR THE FIFTEEN DAYS DURING WHICH HE WAS UNDER OBSERVATION

The fifteen days during which Weston was under observation were divided into three periods of five days each. During the first period of five days, he took very moderate exercise and assumed to be "training" for the walk, though he did not pursue the system generally adopted in training for feats of endurance. The second period embraces the five days of the walk. The third period of five days after the walk was one of almost absolute rest. During the entire fifteen days he abstained altogether from alcoholic beverages. Though not what is called a total abstainer, Weston is not an habitual drinker. He occasionally takes a glass of ale or wine, but this is rare. During the first two periods Weston did not smoke. He smoked five to seven cigars daily during the third period of five days. In the records of food taken, the time of eating is stated, but I have not thought it necessary to extend the tables by giving a separate account of each meal and shall generally give in a single table the entire quantity consumed in the twenty-four hours.

At the time of making the walk Weston was thirty-one years and eight months old. His height is five feet and seven inches. His ordinary weight, naked, is one hundred and twenty to one hundred and twenty-five pounds. He has never had any serious illness, with the exception of what he describes as vertigo and rather serious brain-symptoms after attempting a walk when he was suffering from a cold and headache. This occurred in the summer

of 1870. He does not know that he has any hereditary tendency to disease.

His general build is slight and the parts above the waist are very light. The bones of the chest and upper extremities are small and the muscles are but little developed. The pelvis is unusually broad for a male, and the lower extremities are so formed that there is a considerable space between the thighs from the knees to the perineum. The lower extremities are remarkable for the unusual development of the muscles that move the thighs upon the pelvis. In walking, it is observed that Weston makes great use of these muscles and uses the muscles of the leg very little. The calf of the leg is small; much smaller than one would expect to see in a pedestrian.

A noticeable peculiarity about the muscles of the thighs and legs is that they never become very hard. They were quite soft before the walk, and at all times during the walk they were in the same condition. It was very remarkable that after the third day when Weston had walked within the twenty-four hours ninety-two miles, the muscles were as soft as ever. It has seemed to me that this peculiarity of the muscles is advantageous. When the muscles are very hard from thorough training, prolonged exertion is likely to produce cramps, due, perhaps, to exaggeration of the normal muscular irritability. This is a difficulty experienced by pedestrians. In the case of Weston, the movements were always free, and, according to his statements, he was never much fatigued. Only once during the five days of the walk did he say that he was "leg-weary." What he complained of most was want of sleep, and at one time, vertigo. The conformation of the feet is perfect; the toes are straight, the instep is high, and the heel is very long, giving a remarkable leverage for the tendo Achillis. The heel does not project, as in the negro, but the tendo Achillis passes straight to the calf of the leg.

The nervous element seemed to me very important in the tasks accomplished by Weston. On the fourth day of the walk, having made on the first day, eighty miles, on the second, forty-eight miles, and on the third, ninety-two miles, he kept on the track after having walked more than fifty miles, until vertigo became so great that he could not see to turn the corners. He was forced to abandon hope

of making four hundred miles in five days; but on the fifth day, he appeared again at 10 A. M., and walked more than forty miles.

FIRST PERIOD, FIVE DAYS BEFORE THE WALK

At midnight, November 15, 1870, the observations were begun. At forty minutes past twelve his general condition was as follows:

Weight (naked).....	120.5 lbs. (54 k. 655 grammes.)
Temperature under the tongue.....	98.6° (37° C.).
Pulse (sitting and perfectly tranquil).....	64.
Respirations.....	19.

Immediately after this examination Weston went to bed.

NOVEMBER 16, FIRST DAY

Weston slept well during the night and rose in good health and spirits at 8.15 A. M. He felt well the entire day; took his breakfast at 9.15 A. M.; dinner at 1.10 P. M.; and supper at 7.55 P. M. He walked during the day about fifteen miles. Though feeling well he was worried and anxious about the business arrangements for his walk. He did not go to bed until 2.35 A. M., November 17. He slept, during the twenty-four hours, seven hours and thirty minutes.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak.....	12.25	187.58
Mutton-chops.....	3.00	45.94
Eggs.....	2.76	22.94
Milk.....	7.21	20.82
Bread.....	9.88	47.48
Potatoes.....	8.25	11.99
Butter.....	2.12	5.94
Sugar.....	1.78	00.00
Coffee.....	35.60	17.13
Tea.....	16.03	1.40
Water.....	24.00	00.00
Salt.....	0.09	00.00
Pepper.....	0.02	00.00
	122.99	361.22
	(3,492.17 grammes.)	(23,404 grammes.)
Total ingesta.....	(7 lbs., 10 $\frac{1}{16}$ oz.)	
Liquids.....	(5 lbs., 2 $\frac{3}{8}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity.....	39.55 fl $\frac{3}{4}$	(1,170.0 cc.)
Specific gravity.....	1024.0	
Urea.....	650.08 grains,	42.120 grammes.
Nitrogen in urea.....	303.37 "	19.656 "
Uric acid.....	3.55 "	0.230 "
Phosphoric acid.....	51.46 "	3.334 "
Sulphuric acid.....	38.37 "	2.486 "
Chloride of sodium.....	195.02 "	12.636 "

This urine presented a light flocculent sediment, which contained a large number of octahedra of oxalate of lime.

FECES

Quantity.....	3.70 oz. av.	105.0 grammes.
Nitrogen.....	19.89 grains,	1.289 "
Nitrogen in urea and feces combined..	323.26 "	20.945 "
Nitrogen of urea and feces per 100 parts of nitrogen of food..		89.49 parts.
Uric acid per 100 parts of urea.....		0.538 "
10.30 P. M.	{ Weight (naked)..... 120.5 lbs. (54 k. 655 grammes.)	
	{ Temperature under the tongue..... 99.7° (37° C.)	
	{ Pulse, full and soft..... 75.	
	{ Respirations..... 20.	

NOVEMBER 17, SECOND DAY

After going to bed at 2.35 A. M., Weston rose at 8.45 A. M. He had a little headache in the middle of the day. He took breakfast at 9.40 A. M.; dinner at 2.30 P. M.; and supper at 7.40 P. M. He walked during the day about five miles. He went to bed at 11.30 P. M. He slept, during the twenty-four hours, six hours and forty minutes.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak.....	5.25	80.39
Roast beef.....	5.25	80.39
Eggs.....	4.14	34.41
Milk ..	4.63	13.37
Bread.....	8.50	40.16
Potatoes.....	10.00	14.44
Tomatoes (stewed)...	7.00	00.00
Butter.....	2.95	8.26
Sugar.....	1.25	00.00
Coffee.....	32.32	15.53
Tea.....	16.03	1.40
Water ..	8.00	00.00
Salt.....	0.02	00.00
Pepper.....	0.09	00.00
	105.43 (2,987.92 gms.)	288.35 (18.682 gms.)
Total ingesta (6 lbs., 9 $\frac{1}{16}$ oz.). Liquids (3 lbs., 12 $\frac{1}{16}$ oz.).		

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity.....	38.03 fl $\frac{3}{4}$	(1,125.0 cc.)
Specific gravity.....	1024.4	
Urea.....	590.35 grains,	38.250 grammes.
Nitrogen in urea.....	275.50 "	16.517 "
Uric acid.....	4.03 "	0.261 "
Phosphoric acid.....	44.08 "	2.921 "
Sulphuric acid.....	40.92 "	2.651 "
Chloride of sodium.....	158.00 "	10.237 "

The sediment was the same as on November 16, but the octahedra of oxalate of lime were more abundant.

FECES

Quantity.....	4.78 oz. av.	135.5 grammes.
Nitrogen.....	25.68 grains,	1.664 "
Nitrogen in urea and feces combined..	301.18 "	18.181 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.	104.45	parts.
Uric acid per 100 parts of urea.....	0.683	"

11.20 P. M.	{ Weight (naked).....	121.25 lbs. (55 kilos.)
	{ Temperature under the tongue.....	98.4° (36.9° C.)
	{ Pulse	73.
	{ Respirations.....	20.

NOVEMBER 18, THIRD DAY

Weston rose at 9 A. M.; took his breakfast at 9.50 A. M.; dinner at 2.15 P. M.; and supper at 7.35 P. M. He said he felt "splendid" all day. He wrote about seven hours and walked about five miles. He was very cheerful all day and went to bed at 12.20 A. M., November 19. He slept, during the twenty-four hours, nine hours.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak.....	10.37	158.79
Eggs.....	2.76	22.94
Milk.....	7.21	20.82
Bread.....	7.75	36.62
Potatoes.....	5.13	7.41
Butter.....	3.13	8.76
Sugar.....	1.75	00.00
Coffee.....	32.32	15.53
Tea.....	16.03	1.40
Salt.....	0.09	00.00
Pepper.....	0.02	00.00
	86.56	272.27
	(2,453.67 grammes.)	(17.641 grammes.)
Total ingesta.....	(5 lbs., 6 $\frac{11}{16}$ oz.)	
Liquids.....	(3 lbs., 7 $\frac{8}{16}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity.....	46.15 fl $\frac{3}{4}$	(1,365.0 cc.)
Specific gravity.....	1023.1	
Urea.....	653.08 grains,	42.315 grammes.
Nitrogen in urea.....	304.77 "	19.747 "
Uric acid.....	0.94 "	0.061 "
Phosphoric acid.....	45.14 "	2.925 "
Sulphuric acid.....	38.86 "	2.518 "
Chloride of sodium.....	191.70 "	12.421 "

There was a rather light cloudy sediment which contained a little mucus and a very few small octahedra of oxalate of lime.

FECES

Quantity.....	4.76 oz. av.	135.0 grammes.
Nitrogen.....	25.59 grains,	1.658 "
Nitrogen in urea and feces combined..	330.36 "	21.405 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.		121.30 parts.
Uric acid per 100 parts of urea.....		0.144 "

11.55 P. M.	Weight (naked).....	120 lbs. (54 k. 432 grammes.)
	Temperature under the tongue.....	98° (36.7° C.)
	Pulse.....	71.
	Respirations.....	20.

NOVEMBER 19, FOURTH DAY

Weston rose at 8.35 A. M., feeling as well as possible; took breakfast at 9 A. M.; dinner at 4.45 P. M.; and supper at 10.45 P. M. He said he felt "splendid" all day. He walked during the day about fifteen miles, was very cheerful and went to bed at 12.45 A. M., November 20. He slept, during the twenty-four hours, seven hours and fifteen minutes.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE 24 HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak	4.25	65.08
Mutton-chops	4.88	74.72
Roast beef	4.88	74.72
Eggs	4.14	34.41
Milk.....	4.38	12.65
Bread.	10.25	48.43
Potatoes.....	0.88	1.27
Butter	2.43	6.80
Sugar.....	1.61	00.00
Coffee.....	32.32	15.53
Tea.....	16.03	1.40
Salt.....	0.09	00.00
Pepper.....	0.05	00.00

86.19 335.01
(2,443.19 grammes.) (21.706 grammes.)

Total ingesta (5 lbs., 6 $\frac{1}{8}$ oz.). Liquids (4 lbs., 4 $\frac{7}{8}$ oz.).

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE		
Quantity.....	32.45 fl $\frac{3}{4}$	(960.0 cc.)
Specific gravity.....	1027.6	
Urea.....	607.55 grains,	39.365 grammes.
Nitrogen in urea.....	283.52 "	18.370 "
Uric acid.....	1.06 "	0.069 "
Phosphoric acid.....	67.00 "	4.341 "
Sulphuric acid.....	51.50 "	3.337 "
Chloride of sodium.....	106.68 "	6.912 "

This urine presented a copious fawn-colored sediment which cleared up with gentle heat. It contained the amorphous urates with a large number of octahedra of the oxalate of lime.

FECES		
Quantity.....	3.17 oz. av.	90.0 grammes.
Nitrogen.....	17.05 grains,	1.105 "
Nitrogen in urea and feces combined..	300.57 "	19.475 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.		89.75 parts.
Uric acid per 100 parts of urea.....		0.174 "
Weight (naked), taken at 12.35 A. M., November 20,	118.5 (53 k.	745 grammes).
11.55 P. M.	{ Temperature under the tongue..... 99.1° (37.3° C.)	
	{ Pulse..... 78.	
	{ Respirations..... 23.	

NOVEMBER 20, FIFTH DAY

Weston rose at 10.45 A. M., feeling remarkably well. He took breakfast at 11.30 A. M.; dinner at 5.55 P. M.; and supper at 11.15 P. M. He said he felt "splendid" all day. He walked about one mile during the day. He started on his walk at 12.15 A. M., November 21. He slept, during the twenty-four hours, ten hours.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE 24 HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak.....	18.25	279.45
Eggs.....	6.90	57.35
Milk.....	11.33	32.71
Bread.....	8.88	41.96
Potatoes.....	3.00	4.43
Butter.....	2.75	7.70
Sugar.....	1.75	00.00
Coffee.....	32.32	15.53
Tea.....	16.03	1.40
Salt.....	0.08	00.00
Pepper.....	0.05	00.00
	101.34	440.43
	(2,872.63 grammes.)	(28.536 grammes.)

Total ingesta (6 lbs., 5 $\frac{1}{16}$ oz.). Liquids (3 lbs., 11 $\frac{1}{16}$ oz.).

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE			
Quantity.....	34.00 fl $\frac{3}{4}$	(1.050.0 cc.)	
Specific gravity.....	1025.2.		
Urea.....	640.13 grains,	41.475	grammes.
Nitrogen in urea.....	298.73 "	19.355	"
Uric acid.....	1.73 "	0.112	"
Phosphoric acid.....	43.01 "	2.787	"
Sulphuric acid.....	38.18 "	2.474	"
Chloride of sodium.....	145.85 "	9.450	"

This specimen of urine presented rather a faint cloudy sediment which contained a large number of octahedra of the oxalate of lime.

FECES			
Quantity.....	3.97 oz. av.	112.5	grammes.
Nitrogen.....	21.33 grains,	1.382	"
Nitrogen in urea and feces combined..	320.06 "	20.737	"
Nitrogen of urea and feces per 100 parts of nitrogen of food.	72.67	parts.	
Uric acid per 100 parts of urea.....	0.270	"	
11.45 P. M.	{ Weight (naked)..... 119.2 lbs. (54 k. 62 grammes.)		
	{ Temperature under the tongue..... 99.5° (37.5°C)		
	{ Pulse..... 93.		
	{ Respirations..... 25.		

SECOND PERIOD, FIVE DAYS OF THE WALK

The walk took place in a large building of corrugated iron, known as the "Empire Skating Rink," on Third Avenue, near Sixty-fourth Street. This building is oblong, measuring 170 by 350 feet. A track made of boards covered with dirt and fine shavings was laid out in the form of a parallelogram. This track was measured by Mr. Joseph L. T. Smith, surveyor, in the presence of Prof. Doremus and myself. The circuit, taken two and a half feet from the inside, measured 735 $\frac{3}{4}$ feet. This measurement was made with a metallic tape, adjusted for temperature and tested in our presence. In making the measurement, Prof. Doremus was at one end of the tape and I was at the other, and every reading was carefully verified. Seven full circuits and 129 $\frac{1}{4}$ additional feet made a full mile. In computing the walk the distance was noted by circuits. Three judges were in attendance day and night; one calling the time of each circuit, and two checking off the circuits in a book provided for that purpose. In addition, either Prof. Doremus, Prof. Mott or I was constantly present. Weston had retiring-rooms in the front

of the building, where his food was prepared, where he slept and where our observations were taken. The distance from the judges' stand to the door of these rooms was $145\frac{1}{10}$ feet.

During the walk Weston took but few regular meals, a great part of his nourishment being taken while actually walking. In this way he took beef-essence, soft-boiled eggs, gruel, tea, coffee and all other drinks. I shall not, therefore, give the time of the meals taken during this period, but simply state the entire quantity consumed in each twenty-four hours.

In regard to the distance walked, we are all satisfied that there is no room for doubt. But although the task proposed was not accomplished, the effort was so great, that I have thought it best to give the history of these five days rather fully in detail.

NOVEMBER 21, FIRST DAY

The following is a summary of the twenty-four hours of November 21:

12 00 to 12 15 A. M.	15 minutes' rest before starting.
12 15 to 4 9 "	3 h. 54 m. walking 20 miles, with 4 stops for urination, averaging 24 sec. each.
4 9 to 7 58 "	3 h. and 49 m. rest (sleep).
7 58 to 9 6 "	1 h. and 8 m. walking $5\frac{1}{2}$ miles.
9 6 to 9 19 "	13 m. for breakfast.
9 19 A. M. to 1 P. M.	3 h. and 41 m. walking 17 miles, with 5 m. 12 sec. for defecation, and 2 stops for urination, averaging 30 sec. each.
1 00 to 1 46 "	46 m. for dinner.
1 46 to 3 25 "	1 h. and 39 m. walking 8 miles, with 2 stops for urination, averaging $27\frac{1}{2}$ sec. each.
3 25 to 3 32 "	7 minutes' rest, sitting on the track.
3 32 to 5 34 "	2 h. and 2 m. walking $9\frac{1}{2}$ miles, with 2 stops for urination, averaging $26\frac{1}{2}$ sec. each.
5 34 to 6 27 "	53 minutes' rest (supper).
6 27 to 8 38 "	2 h. and 11 m. walking 12 miles, with 3 stops for urination, averaging 26 sec. each.
8 38 to 8 48 "	10 minutes' rest, sitting on the track.
8 48 to 10 32 $\frac{1}{2}$ "	1 h. $44\frac{1}{2}$ m. walking 8 miles, with 2 stops for urination, averaging $32\frac{1}{2}$ sec. each.
10 32 $\frac{1}{2}$ to 12 00 "	1 h. $27\frac{1}{2}$ minutes' rest, continued into November 22, 4 h. 58 m.

During the 24 hours of November 21, Weston walked 80 miles in 16 h. and 20 m., including 5 m. 12 sec. for defecation and 6 m. 45 sec. for urination. Deducting the time for defecation and urination, his walking-time was 16 h. 8 m. and 3 sec., and he averaged a fraction less than 5

miles per hour. He had 17 minutes' rest, sitting by the track, and 7 h. and 23 m. for breakfast, dinner, supper and sleep. He urinated 15 times on the track. He vomited a little liquid twice during the night at 10.50 and 11.15. He slept, during the twenty-four hours, about 1 hour.

Walking 80 miles....	16 h.	8 m.	3 sec.
Defecation.....		5 "	12 "
Urination.....		6 "	45 "
Rest on the track....		17 "	
Rest off the track....	7 h.	23 "	
	23 h.	59 m.	60 sec. = 24 hours.

During the whole of the first day, Weston seemed to feel very well and made his walk with ease. He was slightly nauseated at times, but he said that he had always more or less disturbance of that kind when he first began a walk.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Mutton-chops.....	2.00	30.62
Eggs.....	6.90	57.35
Milk.....	5.66	16.34
Bread.....	1.25	5.91
Butter.....	2.63	7.36
Sugar.....	1.63	00.00
Coffee.....	67.67	32.57
Tea.....	16.03	1.40
Water.....	6.75	00.00
Lemonade.....	71.16	00.00
Molasses-and-water ..	4.40	00.00
Salt.....	0.08	00.00
Pepper.....	0.05	00.00
Bicarbonate of potash.	0.04	00.00
	186.25	151.55
	(5,282.38 grammes.)	(9,820 grammes.)
Total ingesta.....	(11 lbs., 10 $\frac{81}{100}$ oz.)	
Liquids.....	(10 lbs., 11 $\frac{61}{100}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE		
Quantity.....	42.09 fl $\frac{3}{4}$	(1,245.0 cc.)
Specific gravity.....	1028.6	
Urea.....	710.00 grains,	46.065 grammes.
Nitrogen in urea.....	331.33 "	21.497 "
Uric acid.....	0.32 "	0.021 "
Phosphoric acid.....	84.95 "	5.504 "
Sulphuric acid.....	73.39 "	4.755 "
Chloride of sodium.....	96.00 "	6.220 "

This specimen of urine presented rather a faint cloudy sediment which contained a large number of octahedra of the oxalate of lime.

FECES

Quantity.....	4.80 oz. av.	136.0 grammes.
Nitrogen.....	25.77 grains,	1.670 "
Nitrogen in urea and feces combined..	357.10 "	22.167 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.	235.63 parts.	
Uric acid per 100 parts of urea.....	0.045 "	
10.40 P. M.	{ Weight (naked) 116.5 lbs. (52 k. 838 grammes.) Temperature under the tongue..... 95.3° (35.3° C.) Pulse..... 98. Respirations 20.	

NOVEMBER 22, SECOND DAY

The following is a summary of the twenty-four hours of November 22:

12 00 to 4 58 A. M.	4 h. and 58 m. rest, continued from November 21, before starting, making, during the night of the 21st and 22d, 6 h. and 25½ m.
4 58 to 6 58 "	2 h. walking 8¼ miles, with 1 stop of 6 m. for defecation.
6 58 to 7 8 "	10 m. rest, sitting on the track.
7 8 to 7 33 "	25 m. walking 1¼ miles.
7 33 to 9 5 "	1 h. and 32 m. rest (breakfast).
9 5 to 11 12 "	2 h. and 7 m. walking 9¾ miles, with 2 stops for urination, averaging 32 sec. each.
11 12 to 11 27 "	15 m. rest, sitting on the track.
11 27 to 1 41 P. M.	2 h. and 14 m. walking 10 miles, with 2 m. rest and 2 stops for urination, averaging 29 sec. each.
1 41 to 1 55 "	14 m. rest, sitting on the track.
1 55 to 4 5 "	2 h. and 10 m. walking 10 miles, with 1 stop for urination, of 25 sec.
4 5 to 10 24 "	6 h. 19 m. Stopped for sleep but dozed only. Ate supper before starting again.
10 24 to 12, less 49 sec.	Walking 8 miles in 1 h. 36 m. less 49 sec. on his walk of 112 miles in 24 h. and continued walking into November 23.

During the 24 hours of November 22, Weston walked 48 miles in 10 h. and 32 m., including 6 m. for defecation and 2 m. 27 sec. for urination. Deducting the time for defecation and urination, his walking-time was 10 h. 23 m. and 33 sec., and he averaged about 4.62 miles per hour. He had 39 minutes' rest, sitting on the track, and 12 h. and 49 m. for breakfast, dinner, supper and sleep. He urinated 5 times on the track. When he stopped at 4.05 P. M. he was undressed, wrapped in a long red-flannel gown and a blanket, carried to a vehicle and driven about five blocks to a private house to sleep. He says that he did not sleep, but dozed and got no rest. About 9.30 P. M. he was brought back to the rink in the way he was taken out, ate supper and began at 10.24 P. M. his first attempt to walk one hundred and twelve miles in twenty-four consecutive hours. He slept, during the twenty-four hours, 4 hours and 28 minutes.

EXCRETION OF NITROGEN

Walking 48 miles..	10 h.	23 m.	33 sec.
Defecation.....		6 "	
Urination.....		2 "	27 "
Rest on the track..		39 "	
Rest off the track..	12 "	49 "	
	22 h.	119 m.	60 sec. = 24 hours.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Roast beef.....	4.00	61.25
Chicken.....	2.25	34.45
Eggs.....	8.28	68.82
Milk.....	5.66	16.34
Bread.....	10.50	49.61
Potatoes.....	2.00	2.89
Butter.....	0.50	1.40
Sugar.....	1.75	00.00
Coffee.....	57.82	27.83
Tea.....	38.08	3.33
Lemonade.....	34.84	00.00
Salt.....	0.08	00.00
Pepper.....	0.05	00.00
	165.81	265.92
	(4,700.13 grammes.)	(17,229 grammes.)
Total ingesta.....	(10 lbs., 5 $\frac{81}{100}$ oz.)	
Liquids.....	(8 lbs., 8 $\frac{40}{100}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity.....	33.50 fl $\frac{2}{3}$	(991.0 cc.)
Specific gravity.....	1030.0.	
Urea.....	702.86 grains,	45.540 grammes.
Nitrogen in urea.....	328.00 "	21.252 "
Uric acid.....	0.14 "	0.009 "
Phosphoric acid.....	72.14 "	4.674 "
Sulphuric acid.....	56.90 "	3.687 "
Chloride of sodium.....	91.68 "	5.940 "

This specimen of urine presented rather a faint, cloudy sediment, which contained a large number of octahedra of the oxalate of lime.

FECES

Quantity.....	7.94 oz. av.	225.0 grammes.
Nitrogen.....	42.64 grains,	2.763 "
Nitrogen in urea and feces combined..	370.64 "	24.015 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.		139.39 parts.
Uric acid per 100 parts of urea.....		0.020 "

10 P. M.	{	Weight (naked).....	116.25 lbs. (52 k. 724 grammes.)
		Temperature under the tongue.....	94.8° (34.9° C.)
		Pulse.....	93.
		Respirations.....	23.

NOVEMBER 23, THIRD DAY

The following is a summary of the twenty-four hours of November 23:

12 00 to	6 6 A. M.	6 h. and 6 m. walking 27 $\frac{1}{4}$ miles, with one stop of 4 m. 30 sec. for rest, and 4 stops for urination, averaging 30 $\frac{1}{4}$ sec. each.
6 6 to	6 14 "	8 minutes' rest, sitting on the track.
6 14 to	1 31 P. M.	7 h. and 17 m. walking 33 miles, with 4 stops for urination, averaging 31 $\frac{1}{4}$ sec. each.
1 31 to	1 37 "	6 minutes' rest, sitting on the track.
1 37 to	2 24 "	47 m. walking 3 $\frac{3}{4}$ miles, with one stop of 34 sec. for urination.
2 24 to	2 31 "	7 minutes' rest, sitting on the track.
2 31 to	3 5 "	34 m. walking 2 $\frac{3}{4}$ miles.
3 5 to	3 32 "	27 minutes' rest, sitting on the track.
3 32 to	4 46 "	1 h. 14 m. walking 5 $\frac{1}{4}$ miles, including 2 stops for urination, averaging 27 $\frac{1}{4}$ sec. each.
4 46 to	5 16 "	30 minutes' rest, sitting on the track.
5 16 to	5 46 "	30 m. walking 2 miles, with one stop of 58 sec. for urination.
5 46 to	6 49 "	1 h. and 3 m. rest in his room (supper).
6 49 to	9 11 "	2 h. and 22 m. walking 11 miles, with one stop of 30 sec. for urination.
9 11 to	9 21 "	10 minutes' rest, sitting on the track.
9 21 to	10 52 "	1 h. and 31 m. walking 7 miles, with one stop of 43 sec. for urination.
10 52 to	12 00 M.	1 h. and 8 m. rest, continued into November 24.

During the 24 hours of November 23, Weston walked 92 miles in 20 h. and 21 m., including 4 m. 30 sec. rest, and 7 m. 47 sec. for urination. His walking-time was 20 h. 8 m. and 43 sec. and he averaged a fraction more than 4 $\frac{1}{4}$ miles per hour. He had 1 h. 32 m. and 30 sec. rest, sitting on the track, and 2 h. and 11 m. rest in his room. Before 12, midnight, November 22, he had walked 8 miles in 1 h. 35 m. and 11 sec., making 100 miles in 24 h. and 28 m. His last rest of 1 h. and 8 m. was continued into November 24 1 h. and 33 m. He urinated on the track 14 times.

During the early part of the day, Weston seemed cheerful and confident, but after walking about sixty miles, he complained of drowsiness and found it absolutely impossible to make the time necessary to accomplish his hundred and twelve miles in twenty-four consecutive hours. He stated that he was not fatigued, but suffered only from want of sleep. He was not much depressed at his first failure, as he intended to make a second trial of the hundred-and-twelve-mile walk.

He began, 10.24 P. M., November 22, his first attempt to make 112 miles in 24 consecutive hours. He failed on account of want of sleep.

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not having slept well the six hours before the attempt. He had no passage from his bowels during these 24 hours. He slept, during the 24 hours, 30 minutes.

Walking 92 miles	20 h.	8 m.	43 sec.
Urination		7 "	47 "
Rest on the track	1 "	32 "	30 "
Rest off the track	2 "	11 "	
<hr/>			
	23 h.	58 m.	120 sec. = 24 hours.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beef-essence.....	22.26	84.73
Eggs.....	8.28	68.82
Milk.....	6.18	17.84
Bread.....	1.50	7.09
Oatmeal-gruel.....	6.78	2.55
Butter.....	0.50	1.40
Sugar.....	2.00	00.00
Coffee.....	95.95	46.18
Lemonade.....	27.56	00.00
Salt.....	0.08	00.00
Pepper.....	0.05	00.00
	<hr/>	<hr/>
	171.14	228.61
	(4,851.22 grammes.)	(14.812 grammes.)
Total ingesta.....	(10 lbs., 11 $\frac{14}{100}$ oz.)	
Liquids.....	(9 lbs., 14 $\frac{18}{100}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity	40.56 fl $\frac{3}{4}$	(1,200.0 cc.)
Specific gravity	1032.5.	
Urea	851.95 grains,	55.200 grammes.
Nitrogen in urea	397.58 "	25.760 "
Uric acid	4.74 "	0.307 "
Phosphoric acid	102.25 "	6.625 "
Sulphuric acid	63.71 "	4.128 "
Chloride of sodium	44.45 "	2.880 "

This specimen presented a whitish, flocculent and rather copious sediment which contained a large number of octahedra of the oxalate of lime.

NO FECES PASSED

Nitrogen of urea (no feces) per 100 parts of nitrogen of food	173.91 parts.
Uric acid per 100 parts of urea	0.566 "

11.15 P. M.	{ Weight inaccurately taken.....	
	{ Temperature under the tongue..... 96.6° (35.9° C.)	
	{ Pulse (76 at 5 P. M.)..... 109.	
	{ Respirations..... 22.	

NOVEMBER 24, FOURTH DAY

The following is a summary of the twenty-four hours of November 24:

12 00 to	1 33 A. M.	1 h. 33 m. rest in room, continued from November 23, making in all, 2 h. 41 m. rest for the night of November 23 and 24.
1 33 to	4 12 "	2 h. 39 m. walking 23 $\frac{1}{4}$ miles, with 3 m. stop for defecation and 30 sec. for urination.
4 12 to	9 59 "	5 h. and 47 m. rest in room.
9 59 to	2 58 P. M.	4 h. 59 m. walking 23 $\frac{1}{4}$ miles, with 3 stops for urination, averaging 30 $\frac{1}{2}$ sec. each.
2 58 to	3 3 "	5 minutes' rest, sitting on the track.
3 3 to	6 10 "	3 h. and 7 m. walking 14 $\frac{1}{4}$ miles, with 2 stops for urination, averaging 42 $\frac{1}{2}$ sec. each.
6 10 to	6 13 "	3 minutes' rest, sitting on the track.
6 13 to	6 29 "	16 m. walking 1 $\frac{1}{4}$ miles, with 30 sec. for urination.
6 29 to	6 39 "	10 minutes' rest, sitting on the track.
6 39 to	6 51 "	12 m. walking 1 mile.
6 51 to	7 03 "	12 minutes' rest in his room.
7 03 to	7 10 "	7 m. walking $\frac{1}{4}$ of a mile.
7 10 to	8 06 "	56 minutes' rest in his room.
8 06 to	8 16 "	10 m. walking $\frac{1}{4}$ of a mile, with 40 sec. for urination.
8 16 to	8 21 "	5 minutes' rest, sitting on the track.
8 21 to	8 54 "	33 m. walking 2 $\frac{1}{4}$ miles.
8 54 to	9 2 "	8 minutes' rest, sitting on the track.
9 2 to	9 21 "	19 m. walking 1 $\frac{1}{4}$ miles.
9 21 to	9 31 "	10 minutes' rest, sitting on the track.
9 31 to	9 48 "	17 m. walking 1 mile, with 50 sec. for urination.
9 48 to	10 21 "	33 minutes' rest in room.
10 21 to	10 30 "	9 m. walking $\frac{1}{4}$ of a mile.
10 30 to	12 00 M.	1 h. and 30 m. rest in room, continued into November 25.

During the 24 hours of November 24, Weston walked 57 miles in 12 h. and 48 m., including 3 m. for defecation, and 5 m. and 26 sec. for urination. His walking-time was 12 h. 39 m. and 34 sec., averaging almost exactly 4 $\frac{1}{4}$ miles per hour. He had 41 m. rest, sitting on the track, and 10 h. and 31 m. rest in his room. He urinated on the track 10 times. His last rest, 1 h. and 30 m., was continued into November 25, for 9 h. 56 m., making, during the night of November 24 and 25, 11 h. 26 m. rest.

He began, at 10.13 A. M., his second attempt to walk 112 miles in 24 consecutive hours. At 6.51 P. M. he became very dizzy. This increased so that he staggered and could hardly see the track. After 6 rests and 6 attempts to continue his walk, he was forced to abandon the attempt at 10.30 P. M. He was excessively depressed at his failure, as it was then impossible for him to accomplish the four hundred miles in five days. He

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took a little food, lay down and went to sleep about midnight. He slept during this twenty-four hours, 1 hour; but his sleep was continued into the next day.

Walking 57 miles.....	12 h.	39 m.	34 sec.
Defecation.....		3 "	
Urination.....		5 "	26 "
Rest on the track.....		41 "	
Rest off the track.....	10 "	31 "	
		22 h.	119 m. 60 sec. = 24 hours.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Roast beef.....	1.62	24.81
Beef-essence.....	10.33	39.32
Milk.....	8.75	25.27
Bread.....	6.62	31.28
Oatmeal-gruel.....	7.92	2.92
Sugar.....	3.62	00.00
Coffee.....	38.38	18.47
Tea.....	30.06	2.63
Lemonade.....	41.60	00.00
Salt.....	0.08	00.00
Pepper.....	0.05	00.00
Bicarbonate of potash.....	0.04	00.00
149.07		144.70
(4,225.61 grammes.)		(9.376 grammes.)
Total ingesta.....	(9 lbs., 5 $\frac{1}{16}$ oz.)	
Liquids.....	(8 lbs., 9 $\frac{1}{16}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity.....	32.52 fl $\frac{3}{4}$	(965.0 cc.)
Specific gravity.....	1029.6.	
Urea.....	688.98 grains,	44.641 grammes.
Nitrogen in urea.....	321.52 "	20.832 "
Uric acid.....	9.21 "	0.597 "
Phosphoric acid.....	66.30 "	4.296 "
Sulphuric acid.....	32.66 "	2.116 "
Chloride of sodium.....	28.78 "	1.865 "

This urine presented a faint deposit like mucus which contained a moderate number of octahedra of the oxalate of lime with a few granules of amorphous urates.

FECES

Quantity.....	5.03 oz. av.	142.5 grammes.
Nitrogen.....	21.01 grains,	1.750 "
Nitrogen in urea and feces combined.	348.53 "	22.582 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.	240.86 parts.	
Uric acid per 100 parts of urea.....		1.336 "

10.40 P. M.	{	Weight (naked).....	114 lbs. (51 k. 704 grammes.)
		Temperature under the tongue.....	96.6° (35.9° C.)
		Pulse.....	68.
		Respirations.....	18.

NOVEMBER 25, FIFTH DAY

The following is a summary of the twenty-four hours of November 25:

12 00 to	9 56 A. M.	9 h. and 56 m. rest before starting, with 1 h. 30 m. of November 24, make 11 h. 26 m. rest for the night of November 24 and 25.
9 56 to	10 11 "	15 m. walking 1 mile.
10 11 to	10 16 "	5 minutes' rest in room.
10 16 to	10 58 "	42 m. walking 3 miles, with 1 m. for urination.
10 58 to	11 21 "	23 minutes' rest, sitting on the track.
11 21 to	11 52 "	31 m. walking 2½ miles.
11 52 to	12 42 P. M.	50 minutes' rest in room.
12 42 to	1 1 "	19 m. walking 1½ mile, with 30 sec. for urination.
1 1 to	2 39 "	1 hour 38 minutes' rest in room.
2 39 to	4 19 "	1 h. 40 m. walking 7 miles, with 25 sec. for urination.
4 19 to	4 34 "	15 minutes' rest in room.
4 34 to	6 19 "	1 h. and 45 m. walking 8 miles, with 2 stops for urination, averaging 29½ sec. each.
6 19 to	7 43 "	1 hour and 24 minutes' rest in room.
7 43 to	9 32 "	1 h. and 49 m. walking 9 miles, with 40 sec. for urination.
9 32 to	9 50 "	18 minutes' rest, sitting on the track.
9 50 to	11 31 "	1 h. and 41 m. walking 7 miles, with 2 stops for urination, averaging 25 sec. each.
11 31 to	11 41 "	10 minutes' rest, sitting on the track.
11 41 to	12 00 M.	19 m. walking 1½ miles.

During the twenty-four hours of November 25, Weston walked 40½ miles in 9 h. and 1 m., including 4 m. and 24 sec. for urination. His walking-time was 8 h. 56 m. and 36 sec., averaging a fraction more than 4½ miles per hour. He had 51 minutes' rest sitting on the track, and 14 h. and 8 m. rest in his room. He urinated on the track 7 times. After 12 M., he was in remarkably fine condition. He made several rounds in less than 1 minute, one round in 54 sec., on his thirtieth mile, which was done in 8 m. 32 sec. He walked about 1 mile from 12 to 12.15 A. M., November 26. At the conclusion of his walk he was in the best of health and spirits. He slept, during the twenty-four hours, 9 hours and 26 minutes.

Walking 40½ miles...	8 h.	56 m.	36 sec.
Urination		4 "	24 "
Rest on the track.....		51 "	
Rest in his room.....	14 "	8 "	
<hr/>			
	22 h.	119 m.	60 sec. = 24 hours.

EXCRETION OF NITROGEN

TOTAL MILES WALKED

Nov. 21	80 miles.
" 22	48 "
" 23	92 "
" 24	57 "
" 25	40½ "
<hr/>	
	317½ miles.

In going thirty-two times to his room, Weston walked, in addition to the above, 0.883 of a mile. From midnight, November 25, to 12.15 A. M., November 26, he walked 1½ miles, to complete his five days. This, with the few feet to the urinal, makes about 320 miles in five consecutive days.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Roast beef.....	3.00	45.94
Chicken.....	11.00	168.44
Beef-essence.....	9.54	36.31
Eggs.....	4.14	34.41
Milk.....	9.78	28.24
Bread....	9.00	42.52
Potatoes.....	4.00	5.77
Oatmeal-gruel.....	3.39	1.28
Butter.....	1.25	3.50
Sugar.....	2.37	00.00
Tomatoes.....	3.12	00.00
Coffee.....	27.27	13.12
Tea.....	40.08	3.51
Lemonade.....	52.00	00.00
Water.....	5.00	00.00
Salt.....	0.08	00.00
Pepper.....	0.05	00.00
<hr/>		
	185.07	383.04
	(5,246.09 grammes.)	(24,818 grammes.)
Total ingesta.....	(11 lbs., 9½ oz.)	
Liquids.....	(9 lbs., 7½ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE		
Quantity.....	43.60 fl ⅔	(1,290.0 cc.)
Specific gravity.....	1022.6.	
Urea.....	657.02 grains,	42.570 grammes.
Nitrogen in urea.....	306.61 "	19.866 "
Uric acid.....	0.57 "	0.037 "
Phosphoric acid.....	57.49 "	3.725 "
Sulphuric acid.....	40.84 "	2.646 "
Chloride of sodium.....	64.50 "	4.179 "

This urine presented a whitish grumous sediment, rather copious, which contained a few octahedra of the oxalate of lime with a few granules of amorphous phosphates.

FECES

Quantity.....	4.87 oz. av.	138.0 grammes.
Nitrogen.....	26.16 grains,	1.695 "
Nitrogen in urea and feces combined.	332.77 "	21.561 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.	84.27 parts.	
Uric acid per 100 parts of urea.....	0.087 "	
1.30 A. M.	{ Weight (naked)..... 115.75 lbs. (52 k. 497 grammes.) Temperature under the tongue..... 97.9° (36.6° C.) Pulse..... 80. Respirations..... 20.	
Nov. 26.		

THIRD PERIOD, FIVE DAYS AFTER THE WALK

Notwithstanding the muscular and nervous strain to which Weston had subjected himself for the past five days, culminating on the fourth day in complete prostration of the nervous system, he sat up, talked and joked with his friends until 1.40 A. M., November 26, then went to bed and slept well until 10 A. M. He then got up, "feeling splendid," wakening his attendants, who were almost exhausted by the five days' labor and watching, and called for his breakfast, which he ate at 11.45, with excellent appetite. For the succeeding five days he felt as well as ever. During these five days he did absolutely nothing but eat, sleep and amuse himself, attending to no business. He took no exercise, walking only about two miles a day, though he said he felt as if he could walk one hundred miles any day without difficulty. The history of this period closed our investigations.

NOVEMBER 26, FIRST DAY

Weston slept well. He took breakfast at 11.45 A. M. and dinner at 6.45 P. M. He smoked six cigars during the day. He walked two miles. He slept, during the twenty-four hours, eight hours and twenty minutes.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Turkey	7.50	114.84
Chicken.....	5.12	78.40
Fish.....	3.50	53.59
Eggs... ..	4.14	34.41
Milk.....	2.06	5.95
Custard.....	3.25	18.20
Ice-cream.....	3.50	19.60
Bread.....	7.75	36.62

EXCRETION OF NITROGEN

	Oz. Av.	Nitrogen, in grains.
Potatoes.....	5.00	7.22
Butter.....	1.88	5.26
Sugar.....	0.88	00.00
Cauliflower.....	3.00	00.00
Cranberries.....	5.00	00.00
Celery.....	1.00	00.00
Lettuce.....	1.25	00.00
Grapes.....	1.00	00.00
Apples.....	5.00	00.00
Coffee.....	24.24	11.56
Lemonade.....	14.68	00.00
Water.....	30.00	00.00
Salt.....	0.15	00.00
Pepper.....	0.05	00.00
	129.95	385.65
	(3,683.63 grammes.)	(24.987 grammes.)
Total ingesta.....	(8 lbs., 1 $\frac{15}{16}$ oz.)	
Liquids.....	(2 lbs., 14 $\frac{1}{16}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE		
Quantity.....	31.59 fl $\frac{3}{4}$	(937.5 cc.)
Specific gravity.....	1025.8.	
Urea.....	593.23 grains,	38.437 grammes.
Nitrogen in urea.....	276.84 "	17.937 "
Uric acid.....	0.48 "	0.031 "
Phosphoric acid.....	29.06 "	1.883 "
Sulphuric acid.....	49.53 "	3.209 "
Chloride of sodium.....	66.41 "	4.303 "

This urine presented a rather heavy, whitish sediment in considerable quantity which contained granules of the amorphous urates with a very few octahedra of the oxalate of lime.

FECES		
Quantity.....	3.51 oz. av.	99.5 grammes.
Nitrogen.....	18.86 grains,	1.222 "
Nitrogen in urea and feces combined..	295.70 "	19.159 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.	76.68	parts.
Uric acid per 100 parts of urea.....	0.081	"
12.10 A. M.	{ Weight (naked)..... 118 lbs. (53 k. 518 grammes.) Temperature under the tongue..... 98.6° (37° C.) Pulse..... 76. Respirations..... 22.	
Nov. 27.		

NOVEMBER 27, SECOND DAY

Weston slept well. He took breakfast at 10 A. M.; dinner at 2 P. M.; and supper at 6.45 P. M. He smoked seven cigars during the day. He walked about two miles. He slept, during the twenty-four hours, eight hours and fifteen minutes.

EXCRETION OF NITROGEN

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WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak	5.00	76.56
Roast beef	2.50	38.28
Turkey	9.00	137.81
Head-cheese	1.50	14.70
Eggs	4.14	34.41
Milk	5.14	14.87
Bread	16.15	76.31
Cheese	1.13	20.28
Potatoes	10.25	14.82
Oysters	3.90	36.34
Ice-cream	2.88	16.13
Butter	2.75	7.70
Sugar	1.56	00.00
Tomatoes	5.25	00.00
Cranberries	4.50	00.00
Preserves	4.75	00.00
Catsup	0.42	00.00
Coffee	19.19	9.23
Tea	19.04	1.66
Molasses-and-water...	21.45	00.00
Water	40.00	00.00
Salt	0.05	00.00
Pepper	0.06	00.00
	<hr/> 180.61	<hr/> 499.10
	(5,119.66 grammes.)	(32.338 grammes.)
Total ingesta	(11 lbs., 4 $\frac{1}{2}$ oz.)	
Liquids	(6 lbs., 8 $\frac{1}{2}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE

Quantity	46.14 fl $\frac{3}{4}$	(1,365.0 cc.)
Specific gravity	1024.4	
Urea	716.29 grains,	46.410 grammes.
Nitrogen in urea	334.27 "	21.658 "
Uric acid	0.52 "	0.034 "
Phosphoric acid	46.93 "	3.041 "
Sulphuric acid	46.07 "	2.985 "
Chloride of sodium	170.64 "	11.056 "

This urine presented a slight sediment of a whitish appearance which contained a few octahedra of the oxalate of lime and a few groups of small crystals of uric acid.

FECES

Quantity	4.57 oz. av.	129.5 grammes.
Nitrogen	24.54 grains,	1.590 "
Nitrogen in urea and feces combined.	358.81 "	23.248 "
Nitrogen of urea and feces per 100 parts of nitrogen of food.	71.81 parts.	
Uric acid per 100 parts of urea	0.072 "	

EXCRETION OF NITROGEN

11 P. M.	{	Weight (naked).....	120.25 lbs. (54 k. 539 grammes.)
		Temperature under the tongue.....	98.4° (36.9° C.)
		Pulse.....	73.
		Respirations.....	22.

NOVEMBER 28, THIRD DAY

Weston slept well. He took breakfast at 8.50 A. M.; dinner at 4.15 P. M.; and supper at 7.45 P. M. He smoked five cigars during the day. He walked about two miles. He slept, during the twenty-four hours, eight hours and fifty minutes.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE 24 HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak.....	9.37	143.48
Oysters.....	5.62	53.37
Eggs.....	4.14	34.41
Milk.....	9.27	26.76
Cream-cakes.....	3.37	18.97
Bread.....	11.62	54.80
Cheese.....	1.25	22.53
Potatoes.....	11.00	15.88
Butter.....	2.75	7.70
Sugar.....	2.78	00.00
Tomatoes.....	3.75	00.00
Sweet pickles.....	2.18	00.00
Apples.....	3.12	00.00
Grapes.....	2.75	00.00
Coffee.....	32.32	15.53
Tea.....	16.03	1.40
Salt.....	0.06	00.00
Pepper.....	0.06	00.00
Vinegar.....	0.25	00.00
	121.69	394.83
	(3,449.49 grammes.)	(25,582 grammes.)
Total ingesta.....	(7 lbs., 9 $\frac{11}{16}$ oz.)	
Liquids.....	(3 lbs., 9 $\frac{17}{16}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE			
Quantity.....	84.18 fl $\frac{5}{8}$	(2,490.0 cc.)	
Specific gravity.....	1019.7.		
Urea.....	768.61 grains,	49.800 grammes.	
Nitrogen in urea.....	358.68 "	23.240 "	
Uric acid.....	0.31 "	0.020 "	
Phosphoric acid.....	105.68 "	6.847 "	
Sulphuric acid.....	53.57 "	3.471 "	
Chloride of sodium.....	622.58 "	40.338 "	

This urine presented a slight sediment of a whitish appearance which contained a few octahedra of the oxalate of lime and a few groups of small crystals of uric acid.

FECES

Quantity.....	9.53 oz. av.	270.0 grammes.
Nitrogen.....	51.19 grains,	3.316 "
Nitrogen in urea and feces combined.	409.87 "	26.556 "
Nitrogen in urea and feces per 100 parts of nitrogen of food.	103.81	parts.
Uric acid per 100 parts of urea.....	0.040	"
10.30 P. M.	{ Weight (naked)..... 120.25 lbs. (54 k. 539 grammes.)	
	{ Temperature under the tongue..... 99.3° (37.4° C.)	
	{ Pulse..... 70.	
	{ Respirations..... 22.	

NOVEMBER 29, FOURTH DAY

Weston slept well. He took breakfast at 9.35 A. M.; dinner at 2 P. M.; supper at 6.30 P. M.; and a second supper (which weighed 3 lbs., 6.75 oz. av.) at 11.15 P. M. He smoked five cigars during the day. He walked about two miles. He slept, during the twenty-four hours, seven hours and thirty-five minutes.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak.....	4.25	65.08
Roast beef.....	2.75	42.11
Chicken.....	15.00	229.69
Eggs.....	4.14	34.41
Milk.....	6.25	18.05
Bread.....	18.63	88.03
Potatoes.....	13.50	20.59
Cheese.....	1.00	18.03
Rice-pudding.....	14.75	77.15
Butter.....	5.12	14.33
Sugar.....	2.12	00.00
Tomatoes.....	7.38	00.00
Tomato-soup.....	8.00	00.00
Celery.....	1.00	00.00
Figs.....	2.37	9.54
Apples.....	7.00	00.00
Coffee.....	48.48	23.30
Tea.....	16.03	1.40
Water.....	10.00	00.00
Salt.....	0.16	00.00
Pepper.....	0.08	00.00
	188.01	641.71
	(5,329.43 grammes.)	(41,578 grammes.)
Total ingesta.....	(11 lbs., 12 $\frac{1}{8}$ oz.)	
Liquids.....	(5 lbs., 8 $\frac{1}{16}$ oz.)	

EXCRETION OF NITROGEN

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE			
Quantity.....	60.38 fl $\frac{3}{4}$	(1,786.0 cc.)	
Specific gravity.....	1022.5.		
Urea.....	744.32 grains,	48.226 grammes.	
Nitrogen in urea.....	347.35 "	22.505 "	
Uric acid.....	2.51 "	0.163 "	
Phosphoric acid.....	50.76 "	3.289 "	
Sulphuric acid.....	48.73 "	3.157 "	
Chloride of sodium.....	297.70 "	19.288 "	

This urine presented hardly any sediment. The microscopical examination was entirely negative.

FECES			
Quantity.....	6.61 oz. av.	187.5 grammes.	
Nitrogen.....	35.54 grains,	2.303 "	
Nitrogen in urea and feces combined.	382.89 "	24.808 "	
Nitrogen of urea and feces per 100 parts of nitrogen of food.	59.67 parts.		
Uric acid per 100 parts of urea.....	0.337 "		

12.20 A. M. Nov. 30.	Weight * (naked).....	123.5 lbs. (56 k. 13 grammes.)
	Temperature under the tongue.....	98.8° (37.1° C.)
	Pulse.....	78.
	Respirations.....	24.

NOVEMBER 30, FIFTH DAY

Weston slept well. He took breakfast at 9.15 A. M.; dinner at 1.45 P. M.; and supper at 6.15 P. M. He smoked during the day, six cigars. He walked about three miles. He had a headache all the evening. He slept, during the twenty-four hours, seven hours and forty-five minutes. The records were closed at midnight.

WEIGHTS AND ANALYSES OF FOOD AND DRINK FOR THE TWENTY-FOUR HOURS

	Oz. Av.	Nitrogen, in grains.
Beefsteak	1.88	28.79
Roast beef.....	3.37	51.60
Fish.....	3.00	45.94
Milk.....	5.66	16.34
Bread.....	21.00	99.22
Potatoes	5.94	8.58
Butter	4.12	11.54
Sugar.....	1.88	00.00
Tomatoes.....	3.12	00.00
Tomato-soup.....	8.00	00.00
Figs.....	2.06	8.29
Preserved citron.....	2.25	00.00
Coffee.....	24.24	11.65

* This great increase in weight is accounted for by 3 lbs. 6.75 oz. of food taken at 11.15 P. M.

	Oz. Av.	Nitrogen, in grains.
Tea	16.03	1.40
Salt.....	0.06	00.00
Pepper.....	0.06	00.00
	<u>102.67</u>	<u>283.35</u>
	(2,910.34 grammes.)	(18,359 grammes.)
Total ingesta.....	(6 lbs., 6 $\frac{47}{100}$ oz.)	
Liquids.....	(2 lbs., 15 $\frac{18}{100}$ oz.)	

ANALYSES OF EXCRETIONS OF TWENTY-FOUR HOURS

URINE			
Quantity.....	68.39 fl $\frac{3}{4}$	(2,023.0 cc.)	
Specific gravity.....	1022.6.		
Urea.....	811.48 grains,	52.598 grammes.	
Nitrogen in urea.....	378.69 "	24.546 "	
Uric acid.....	3.30 "	0.214 "	
Phosphoric acid.....	52.00 "	3.364 "	
Sulphuric acid.....	47.20 "	3.058 "	
Chloride of sodium.....	404.65 "	26.218 "	

This urine presented a cloudy sediment in moderate quantity which contained a moderate number of octahedra of the oxalate of lime.

FECES			
Quantity.....	7.41 oz. av.	210.0 grammes.	
Nitrogen.....	39.80 grains,	2.579 "	
Nitrogen in urea and feces combined.	418.49 "	27.125 "	
Nitrogen of urea and feces per 100 parts of nitrogen of food.		147.69 parts.	
Uric acid per 100 parts of urea.....		0.406 "	
12 M.	{ Weight (naked).....	120.75 lbs. (54 k. 765 grammes.)	
	{ Temperature under the tongue.....	97.5° (36.4° C.)	
	{ Pulse.....	76.	
	{ Respirations.....	24.	

CONSOLIDATED TABLES

I propose to present, in a series of consolidated tables, the complete history of the fifteen days, divided as before into three periods of five days each, in the form in which they will be made use of in Part II. in making the final deductions. I present them in this form complete, so that all or any part of them may serve as material for the use of others. The cutaneous and pulmonary exhalations were estimated by subtracting the weight of urine and feces from the weight of ingesta; and to this result adding any loss of weight, or subtracting from it any gain in the weight of the body during the twenty-four hours.

The weights are given in pounds and ounces avoirdupois and in grains troy. The equivalents in French weights are given in parentheses:

TABLE A'.—WEIGHT, TEMPERATURE, PULSE, ETC.

FIRST PERIOD—FIVE DAYS BEFORE THE WALK

	First day, November 16.	Second day, November 17.	Third day, November 18.	Fourth day, November 19.	Fifth day, November 20.
Weight of the body (naked).....	120.5 lbs. (54 k. 655 gr.)	121.25 lbs. (55 kilogr.)	120 lbs. (54 k. 432 gr.)	118.5 lbs. (53 k. 745 gr.)	119.2 lbs. (54 k. 62 gr.)
Temperature under the tongue.....	99.7° Fahr. (37.6° C.)	98.4° Fahr. (36.9° C.)	98° Fahr. (36.7° C.)	99.1° Fahr. (37.3° C.)	99.5° Fahr. (37.5° C.)
Pulse (sitting and tranquil).....	75	73	71	78	93
Respirations (sitting and tranquil).....	20	20	20	23	25
Weight of ingesta.....	122.99 oz. (3,492.17 gr.)	105.43 oz. (2,987.92 gr.)	86.56 oz. (2,453.67 gr.)	86.19 oz. (2,443.19 gr.)	101.34 oz. (2,872.63 gr.)
Weights of urine and feces.....	44.20 oz. (1,303.08 gr.)	43.73 oz. (1,287.95 gr.)	51.98 oz. (1,531.53 gr.)	36.51 oz. (1,076.50 gr.)	38.83 oz. (1,188.96 gr.)
Estimated cutaneous and pulmonary exhalation.....	78.79 oz. (2,189.09 gr.)	49.70 oz. (1,354.97 gr.)	54.58 oz. (1,497.14 gr.)	73.58 oz. (2,046.69 gr.)	51.51 oz. (1,366.67 gr.)
Number of hours of sleep.....	7 h. 30 m.	6 h. 40 m.	9 h.	7 h. 15 m.	10 h.
Number of miles walked.....	15	5	5	15	1

TABLE B.¹—WEIGHTS AND ANALYSES OF FOOD AND DRINK

FIRST PERIOD—FIVE DAYS BEFORE THE WALK

	FIRST DAY, NOVEMBER 16.		SECOND DAY, NOVEMBER 17.		THIRD DAY, NOVEMBER 18.		FOURTH DAY, NOVEMBER 19.		FIFTH DAY, NOVEMBER 20.	
	Quantity in ounces.	Nitrogen in grains.	Quantity in ounces.	Nitrogen in grains.	Quantity in ounces.	Nitrogen in grains.	Quantity in ounces.	Nitrogen in grains.	Quantity in ounces.	Nitrogen in grains.
Meats	15.25	233.52	10.50	160.78	10.37	158.79	14.01	214.52	18.25	279.45
Eggs.....	2.76	22.94	4.14	34.41	2.76	22.94	4.14	34.41	6.90	57.35
Milk	7.21	20.82	4.63	13.37	7.21	20.82	4.38	12.65	11.33	32.71
Bread.....	9.88	47.48	8.50	40.16	7.75	36.62	10.25	48.43	8.88	41.96
Potatoes.....	8.25	11.99	10.00	14.44	5.13	7.41	0.88	1.27	3.00	4.33
Butter.....	2.12	5.94	2.95	8.26	3.13	8.76	2.43	6.80	2.75	7.70
Coffee.....	35.60	17.13	32.32	15.53	32.32	15.53	32.32	15.53	32.32	15.53
Tea	16.03	1.40	16.03	1.40	16.03	1.40	16.03	1.40	16.03	1.40
Non-nitrogenous matters....	25.89	16.36	1.86	1.75	1.88
Total.....	122.99	361.22	105.43	288.35	86.56	272.27	86.19	335.01	101.34	440.43
Total in grammes.....	3,492.17	23,404	2,987.92	18,682	2,453.67	17,641	2,443.19	21,706	2,872.63	28,536

Average of five days, quantity of food and drink..... 100.50 oz.
 " " "..... 2,848.82 grammes.
 " " "..... 339.46 grains.
 " " "..... 21,994 grammes.

TABLE C.¹—ANALYSES OF EXCRETIONS—URINE AND FECES
FIRST PERIOD—FIVE DAYS BEFORE THE WALK
(French weights in parentheses)

Urine.	1st day, Nov. 16.	2d day, Nov. 17.	3d day, Nov. 18.	4th day, Nov. 19.	5th day, Nov. 20.	Averages.
Quantity.....	39.55 fl. oz. (1,170.0 cc.)	38.03 fl. oz. (1,125.0 cc.)	46.15 fl. oz. (1,305.0 cc.)	32.45 fl. oz. (960.0 cc.)	34.00 fl. oz. (1,050.0 cc.)	37.84 fl. oz. (1,134.0 cc.)
Specific gravity.....	1024.0	1024.4	1023.1	1027.6	1025.2	1024.9
Urea.....	650.08 grains (42.120)	590.35 grains (38.250)	653.08 grains (42.315)	607.55 grains (39.365)	640.13 grains (41.475)	628.24 grains (40.705)
Nitrogen in urea.....	303.37 (19.656)	275.50 (16.517)	304.77 (19.747)	283.52 (18.370)	298.73 (19.355)	293.18 (18.720)
Uric acid.....	3.55 (0.230)	4.03 (0.261)	0.94 (0.061)	1.06 (0.069)	1.73 (0.112)	2.26 (0.127)
Phosphoric acid.....	51.46 (3.334)	44.08 (2.921)	45.14 (2.925)	67.00 (4.341)	43.01 (2.787)	50.14 (3.262)
Sulphuric acid.....	38.37 (2.486)	40.92 (2.651)	38.86 (2.518)	51.50 (3.337)	38.18 (2.474)	41.57 (2.693)
Chloride of sodium.....	195.02 (12.636)	158.00 (10.237)	191.70 (12.421)	106.68 (6.912)	145.85 (9.450)	159.45 (10.331)
Abnormal matters.....	Large amount of oxalate of lime (octahedra).	Larger amount of oxalate than on Nov. 16.	Small amount of oxalate.	Large amount of oxalate; amor- phous urates.	Large amount of oxalate.	
Feces.						
Quantity.....	3.70 oz. (105.0)	4.78 oz. (135.5)	4.76 oz. (135.0)	3.17 oz. (90.0)	3.97 oz. (112.5)	4.08 oz. (115.6)
Nitrogen in feces.....	19.89 grains (1.289)	25.68 grains (1.664)	25.59 grains (1.658)	17.05 grains (1.105)	21.33 grains (1.382)	21.91 grains (1.421)
Nitrogen in urea and feces combined	323.26 grains (20.945)	301.18 grains (18.181)	330.36 grains (21.405)	300.57 grains (19.475)	320.06 grains (20.737)	315.09 grains (20.149)
N. of urea and feces per 100 pts. N. food	89.49	104.45	121.33	89.72	72.67	92.82
Uric acid per 100 pts. of urea.....	0.538	0.583	0.144	0.174	0.270	0.360

The feces contained an average of 72 per cent. of water.

EXCRETION OF NITROGEN

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TABLE A.²—WEIGHT, TEMPERATURE, PULSE, ETC.
SECOND PERIOD—FIVE DAYS OF THE WALK

	First day, November 21.	Second day, November 22.	Third day, November 23.	Fourth day, November 24.	Fifth day, November 25.
Weight of the body	116.5 lbs. (52 k. 838 gr.)	116.25 lbs. (52 k. 724 gr.)	Estimated 115 lbs. (52 k. 157 gr.)	114 lb.- (51 k. 704 gr.)	115.75 lbs. (52 k. 497 gr.)
Temperature under the tongue.....	95.3° Fahr. (35.3° C.)	94.8° Fahr. (34.9° C.)	96.6° Fahr. (35.9° C.)	96.6° Fahr. (35.9° C.)	97.9° Fahr. (36.6° C.)
Pulse (sitting and tranquil).....	98	93	109	68	80
Respirations (sitting and tranquil).....	20	23	22	18	20
Weight of ingesta.....	186.25 oz.	165.81 oz.	171.14 oz.	149.07 oz.	185.07 oz.
Weights of urine and feces.....	(5,282.38 gr.) 48.09 oz.	(4,700.13 gr.) 42.54 oz.	(4,851.22 gr.) 41.88 oz.	(4,225.61 gr.) 38.51 oz.	(5,246.09 gr.) 49.45 oz.
Estimated cutaneous and pulmonary exhalation.....	(1,416.61 gr.)	(1,245.73 gr.)	(1,239.00 gr.)	(1,136.06 gr.)	(1,457.15 gr.)
Number of hours of sleep.....	181.36 oz. (5,089.78 gr.) 1 h.	127.27 oz. (3,568.40 gr.) 4 h. 28 m. dozed 5 h.	149.26 oz. (4,179.22 gr.) 30 m.	136.56 oz. (3,542.55 gr.) 1 h.	107.62 oz. (2,995.94 gr.) 9 h. 26 m.
Number of miles walked.....	80	48	92	57	40.5
Walking-time.....	16 h. 8 m. 3 s.	10 h. 23 m. 33 s.	20 h. 8 m. 43 s.	12 h. 30 m. 34 s.	8 h. 56 m. 36 s.
Rate per hour.....	about 5 miles.	4.62 miles	about 4.5 miles	4.5 miles	about 4.5 miles
Urination.....	6 m. 45 s.	2 m. 27 s.	7 m. 47 s.	5 m. 26 s.	4 m. 24 s.
Defecation.....	5 m. 12 s.	6 m.	none	3 m.	off the track
Rest on the track.....	1 m.	39 m.	1 h. 32 m. 30 s.	41 m.	51 m.
Rest off the track.....	7 h. 23 m.	12 h. 49 m	2 h. 11 m.	14 h. 8 m.	14 h. 8 m.

TABLE C.³—ANALYSES OF EXCRETIONS—URINE AND FECES
SECOND PERIOD—FIVE DAYS OF THE WALK
(French weights in parentheses)

URINE.	1st day, Nov. 21.	2d day, Nov. 22.	3d day, Nov. 23.	4th day, Nov. 24.	5th day, Nov. 25.	Averages.
Quantity.....	42.09 fl. oz. (1,245.0 cc.)	33.50 fl. oz. (991.0 cc.)	40.56 fl. oz. (1,200.0 cc.)	32.52 fl. oz. (965.0 cc.)	43.60 fl. oz. (1,260.0 cc.)	38.46 fl. oz. (1,138.0 cc.)
Specific gravity.....	1028.6	1030.0	1032.5	1029.6	1022.6	1028.7
Urea.....	710.00 grains (46.065)	702.86 grains (45.540)	851.95 grains (55.200)	688.98 grains (44.641)	657.02 grains (42.570)	722.16 grains (46.803)
Nitrogen in urea.....	331.33 " (21.497)	328.00 " (21.252)	397.58 " (25.760)	321.52 " (20.832)	306.61 " (19.866)	337.01 " (21.841)
Uric acid.....	0.32 " (0.021)	0.14 " (0.009)	4.74 " (0.307)	9.21 " (0.597)	0.57 " (0.037)	3.00 " (0.194)
Phosphoric acid.....	84.95 " (5.504)	72.14 " (4.674)	102.25 " (6.625)	66.30 " (4.206)	57.49 " (3.725)	76.63 " (4.965)
Sulphuric acid.....	73.39 " (4.755)	56.90 " (3.687)	63.71 " (4.128)	32.66 " (2.116)	40.84 " (2.646)	53.50 " (3.666)
Chloride of sodium.....	96.00 " (6.220)	91.68 " (5.940)	44.45 " (2.886)	28.78 " (1.865)	64.50 " (4.179)	65.08 " (4.217)
Abnormal matters.....	Large amount of oxalate of lime (octahedra).	Same as Nov. 21.	Larger amount of oxalate.	Small amount of oxalate.	Small amount of oxalate.	
FECES.						
Quantity.....	4.80 oz. (136.0)	7.94 oz. (225.0)	None	5.03 oz. (142.5)	4.87 oz. (138.0)	4.53 oz. (128.3)
Nitrogen in feces.....	25.77 grains (1.670)	42.64 grains (2.763)	"	27.01 grains (1.750)	26.16 grains (1.695)	24.32 grains (1.576)
Nitrogen in urea and feces combined	357.10 grains (22.167)	370.64 grains (24.015)	397.58 grains (25.760)	348.53 grains (22.582)	332.77 grains (21.561)	361.52 grains (23.217)
N. of urea and feces per 100 pts. N. food	235.63	139.39	173.91	240.86	84.27	153.99
Uric acid per 100 pts. of urea.....	0.045	0.020	0.556	1.336	0.087	0.415

The feces contained an average of 72 per cent. of water.

TABLE A.²—WEIGHT, TEMPERATURE, PULSE, ETC.
THIRD PERIOD—FIVE DAYS AFTER THE WALK

	First day, November 26.	Second day, November 27.	Third day, November 28.	Fourth day, November 29.	Fifth day, November 30.
Weight of the body	118 lbs. (53 k. 518 gr.)	120.25 lbs. (54 k. 539 gr.)	120.25 lbs. (54 k. 539 gr.)	123.5 lbs. (56 k. 13 gr.)	120.75 lbs. (54 k. 765 gr.)
Temperature under the tongue.....	98.6° Fahr. (37° C.)	98.4° Fahr. (36.9° C.)	99.3° Fahr. (37.4° C.)	98.8° Fahr. (37.1° C.)	97.5° Fahr. (36.4° C.)
Pulse (sitting and tranquil).....	76	73	70	78	76
Respirations (sitting and tranquil).....	22	22	22	24	24
Weight of ingesta.....	129.95 oz. (3,683.63 gr.)	180.61 oz. (5,119.66 gr.)	121.69 oz. (3,449.49 gr.)	188.01 oz. (5,339.43 gr.)	102.67 oz. (2,910.34 gr.)
Weights of urine and feces	35.91 oz. (1,061.19 gr.)	51.84 oz. (1,527.81 gr.)	95.37 oz. (2,809.25 gr.)	68.36 oz. (2,013.68 gr.)	77.34 oz. (2,278.72 gr.)
Estimated cutaneous and pulmonary exhalation.....	58.04 oz. (1,601.44 gr.)	92.77 oz. (2,570.85 gr.)	26.32 oz. (640.24 gr.)	67.65 oz. (1,841.75 gr.)	69.33 oz. (1,879.62 gr.)
Number of hours of sleep.....	8 h. 20 m.	8 h. 15 m.	8 h. 50 m.	7 h. 35 m.	7 h. 45 m.
Number of miles walked.....	2	2	2	2	3

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TABLE B.³—WEIGHTS AND ANALYSES OF FOOD AND DRINK
THIRD PERIOD—FIVE DAYS AFTER THE WALK

	FIRST DAY, NOVEMBER 26.	SECOND DAY, NOVEMBER 27.	THIRD DAY, NOVEMBER 28.	FOURTH DAY, NOVEMBER 29.	FIFTH DAY, NOVEMBER 30.
	Quantity in ounces.	Quantity in ounces.	Quantity in ounces.	Quantity in ounces.	Quantity in ounces.
	Nitrogen in grains.	Nitrogen in grains.	Nitrogen in grains.	Nitrogen in grains.	Nitrogen in grains.
Meats N. 3.50 p. c.	16.12	16.50	9.37	22.00	8.25
Eggs N. 1.90 "	4.14	4.14	4.14	4.14
Milk N. 0.66 "	2.06	5.14	9.27	6.25	5.66
Custard N. 1.28 "	3.25	18.20
Ice-cream N. 1.28 "	3.50	19.60
Cream-cakes N. 1.28 "	2.88
Oysters N. 2.13 "	3.90	3.37
Rice-pudding N. 1.18 "	5.62
Head-cheese N. 2.24 "	1.50	14.75
Figs N. 0.92 "	1.00
Cheese N. 4.12 "	1.13	2.37	2.06
Bread N. 1.08 "	7.75	16.15	1.25	22.53
Potatoes N. 0.33 "	5.00	10.25	11.62	54.80	99.22
Butter N. 0.64 "	1.88	2.75	11.00	15.88	8.58
Coffee N. 0.11 "	24.24	19.19	2.75	13.50	5.94
Tea N. 0.02 "	19.04	7.70	5.12	4.12
Non-nitrogenous matters	62.01	78.04	15.53	14.33	11.54
Total	129.95	180.61	14.95	35.74	15.37
Total in grammes	3,683.63	5,119.66	121.69	5,329.43	2,910.34
Average for five days, quantity of food and drink	"	"	394.83	641.71	283.35
" " " Nitrogen	"	"	25.582	41.578	18.359
" " " " " oz. grammes, grains,					
" " " " " 144·59 oz. 4,098·62 grammes, 28·569 grains.					

EXCRETION OF NITROGEN

TABLE C.¹—ANALYSES OF EXCRETIONS—URINE AND FECES
THIRD PERIOD—FIVE DAYS AFTER THE WALK
(French weights in parentheses)

Urine.	1st day, Nov. 26.	2d day, Nov. 27.	3d day, Nov. 28.	4th day, Nov. 29.	5th day, Nov. 30.	Averages.
Quantity.....	31.59 fl. oz. (937.5 cc.)	46.14 fl. oz. (1,305.0 cc.)	84.18 fl. oz. (2,490.0 cc.)	60.38 fl. oz. (1,786.0 cc.)	68.39 fl. oz. (2,023.0 cc.)	58.14 fl. oz. (1,720.3 cc.)
Specific gravity.....	1025.8	1024.4	1019.7	1024.5	1022.6	1023.0
Urea.....	593.23 grains (38.437)	716.29 grains (46.410)	768.61 grains (49.800)	744.32 grains (48.226)	811.48 grains (52.598)	726.79 grains (47.094)
Nitrogen in urea.....	276.84 " (17.937)	334.27 " (21.658)	358.68 " (23.240)	347.35 " (22.505)	378.69 " (24.546)	339.17 " (21.977)
Uric acid.....	0.48 " (0.031)	0.52 " (0.034)	0.31 " (0.020)	2.51 " (0.163)	3.30 " (0.214)	1.42 " (0.082)
Phosphoric acid.....	20.06 " (1.883)	46.93 " (3.041)	105.68 " (6.847)	50.76 " (3.289)	52.00 " (3.364)	56.89 " (3.674)
Sulphuric acid.....	49.53 " (3.209)	46.97 " (2.985)	53.57 " (3.471)	48.73 " (3.157)	47.20 " (3.058)	49.02 " (3.176)
Chloride of sodium.....	66.41 " (4.303)	170.64 " (11.056)	622.58 " (40.338)	297.70 " (19.288)	404.65 " (26.218)	312.40 " (20.241)
Abnormal matters.....	Small amount of lime oxalate of lime (octahedra) ; with amor- phous urates.	Trace of sugar ; small amount of oxalate; uric- acid crystals.	Same as on Nov. 27.	No abnormal matters.	Moderate amount of oxalate.	
Feces						
Quantity.....	3.51 oz. (99.5)	4.57 oz. (129.5)	9.53 oz. (270.0)	6.61 oz. (187.5)	7.41 oz. (210.0)	6.33 oz. (179.3)
Nitrogen in feces.....	18.86 grains (1.222)	24.54 grains (1.590)	51.19 grains (3.316)	35.54 grains (2.303)	39.80 grains (2.579)	33.99 grains (2.202)
Nitrogen in urea and feces combined	295.70 grains (19.159)	358.81 grains (23.248)	499.87 grains (26.556)	382.89 grains (24.808)	418.49 grains (27.125)	373.15 grains (24.179)
N. of urea and feces per 100 pts. N. food	76.68	71.81	103.81	59.67	147.69	84.63
Uric acid per 100 pts. of urea.....	0.081	0.072	0.040	0.337	0.406	0.195

The feces contained an average of 72 per cent. of water.

EXCRETION OF NITROGEN

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TABLE D.—DAILY AVERAGES FOR THE THREE PERIODS
(French weights and measures in parentheses)

	First period—five days before the walk.	Second period—five days of the walk.	Third period—five days after the walk.
Weight.....	Loss in 5 days— 21.8 oz. (593 gr.)	Loss in 5 days— 52.2 oz. (1,565 gr.) Loss in 4 days— 83.2 oz. (2,358 gr.)	Gain in 5 days— 80 oz. (2,268 gr.)
Temperature.....	Average of 5 days— 90° Fahr. (37.2° C.)	Average of 5 days— 96.3° Fahr. (35.7° C.)	Average of 5 days— 98.6° Fahr. (37° C.)
Pulse.....	78	90	74
Respiration.....	22	21	23
Sleep.....	8 h. 5 m.	3 h. 17 m.	8 h. 29 m.
Miles walked.....	8.2 miles	63.5 miles	2.2 miles
Ingesta.....	100.50 oz. (2,848.82 gr.)	171.47 oz. (4,860.57 gr.)	144.59 oz. (4,098.62 gr.)
Nitrogen of food..	339.46 grains (21.994)	234.76 grains (13.211)	440.93 grains (28.569)
Cutaneous and pul- monary exhalation	61.63 oz. (1,690.91 gr.)	138.41 oz. (3,875.18 gr.)	62.82 oz. (1,706.78 gr.)
URINE.			
Quantity.....	37.84 fl. oz. (1,134.0 cc.)	38.46 fl. oz. (1,138.0 cc.)	58.14 fl. oz. (1,720.3 cc.)
Specific gravity....	1024.9	1028.7	1023.0
Urea.....	628.24 grains (40.705)	722.16 grains (46.803)	726.79 grains (47.094)
Nitrogen in urea...	293.18 " (18.729)	337.01 " (21.841)	339.17 " (21.977)
Uric acid.....	2.26 " (0.127)	3.00 " (0.194)	1.42 " (0.082)
Phosphoric acid...	50.14 " (3.262)	76.63 " (4.905)	56.89 " (3.674)
Sulphuric acid....	41.57 " (2.693)	53.50 " (3.666)	49.02 " (3.176)
Chloride of sodium.	159.45 " (10.331)	65.08 " (4.217)	312.40 " (20.241)
FECES.			
Quantity.....	4.08 oz. (115.6)	4.53 oz. (128.3)	6.33 oz. (179.3)
Nitrogen.....	21.91 grains (1.421)	24.32 grains..... (1.576)	33.99 grains (2.202)
Nitrogen in urea and feces combined...	315.09 grains (20.149)	361.52 grains (23.217)	373.15 grains (24.179)
Nitrogen of urea and feces per 100 pts. of nitrogen of food	92.82 parts.....	153.99 parts	84.63 parts
Uric acid per 100 pts. of urea.....	0.360 parts	0.415 parts	0.195 parts

EXCRETION OF NITROGEN

TABLE E.—METEOROLOGICAL OBSERVATIONS, TAKEN AT THE COOPER UNION, NEW YORK CITY, BY PROF. ORAN W. MORRIS

1870. MONTH AND DAY.		BAROMETER.			THERMOMETER (Fahrenheit).				Degree of humidity. Saturation repre- sented by 100.	WIND.		SKY AND ATMOS- PHERE.
		Daily readings corrected and reduced to 32° Fahr.			Self-registering.					General direction.		
		High- est.	Lowest.	Mean.	High- est.	Low- est.	Range	Highest in the sun.		A. M.	P. M.	
Nov.	Date.	in.	in.	in.	°	°	°	°	°			
Wed'day	16	30.065	29.817	29.911	46.0	35.0	11.0	82.0	40.60	NW	S W	Clear.
Thursday	17	30.146	30.059	30.099	47.0	37.0	10.0	78.0	43.16	W	W	Light cl'ds
Friday	18	29.931	29.857	29.895	42.0	29.0	13.0	42.5	61.36	S W	W	Slight rain and slight snow 6.15 P. M.
Saturday	19	29.907	29.735	29.827	36.0	27.0	9.0	42.0	56.66	W	W	Snow squalls. Clear eve.
Sunday	20	29.950	29.932	29.942	43.0	33.0	10.0	74.0	43.20	W	S W	Clear A. M. Cloudy eve.
Monday	21	30.167	29.954	30.029	50.0	38.0	12.0	60.0	44.70	S W	W	Cloudy.
Tuesday	22	30.174	29.623	29.913	48.0	39.8	9.0	48.5	73.70	N E	N E	Rain all day. Gale eve.
Wed'day	23	29.763	29.547	29.624	50.0	36.0	14.0	72.0	51.30	S W	W	Light cl'ds
Thursday	24	29.892	29.832	29.861	44.0	33.0	11.0	77.0	43.46	W	W	Flying clouds.
Friday	25	30.044	29.745	29.879	49.0	39.0	10.0	79.3	48.83	W	S W	Clear A. M. Cl'dy and rain 10.15 P. M.
Saturday	26	29.715	29.477	29.569	50.0	40.0	10.0	82.0	63.13	NW	NW	Rain A. M. Light cl'ds
Sunday	27	29.914	29.803	29.846	58.0	42.0	16.0	89.0	46.40	W	NW	Clear. 2 meteors eve.
Monday	28	30.067	30.054	30.060	58.0	44.0	14.0	90.0	48.90	NW	S W	Light cl'ds
Tuesday	29	30.033	29.811	29.949	62.0	38.0	24.0	88.5	60.76	S W	NW	Light cl'ds Slight rain evening.
Wed'day	30	30.277	30.181	30.221	46.0	34.0	12.0	80.0	46.43	NW	S E	Light cl'ds Clear eve.

The height of the cistern of the barometer is considered to be 46 feet above tide water. A severe gale N. E., and very high tide, on the 22d.

PART II

PHYSIOLOGICAL DEDUCTIONS FROM THE OBSERVATIONS
TAKEN BEFORE, DURING, AND AFTER THE WALK OF
317½ MILES IN FIVE CONSECUTIVE DAYS

The data obtained during the three periods, five days before, five days during and five days after this walk, enable me to come to certain conclusions in regard to physiological questions of interest, particularly the influence of muscular exercise upon the elimination of nitrogen. In regard to the influence of this excessive and prolonged exertion upon the weight of the body, the temperature, circulation, respiration, nervous system, etc., the information is necessarily more incomplete and indefinite. I shall, however, endeavor to make use of the facts that were noted; although the main object was to study the relations of the nitrogen.

The phenomena observed relate to the weight of the body, temperature, pulse and respirations, in so far as these conditions were modified by exercise and sleep. Having taken daily the weights of the ingesta, the excretions by the kidneys and intestines and the weight of the body, it was possible to calculate the amount of exhalation from the lungs and skin.

WEIGHT OF THE BODY

It is well known that by regulating the diet and exercise, the weight may be modified within certain limits; and the system of training employed by athletes is supposed to develop to the highest degree the muscular power and endurance. The principle in training is in brief to regulate the exercise so that gradually the system is worked daily as much as can be endured without exhaustion; and to restrict the diet to rare, lean meats, stale bread and nitrogenous articles, eliminating fatty matters and reducing the starchy matters to a minimum. By this process the weight is reduced—for professional athletes out of training are generally over-weight—the muscles are hardened, nearly all the fat disappears, and the power, and within limits the endurance, are developed to a maximum. In the case of Weston no rigid system of training was adopted; but the

changes in weight are interesting in view of the great variations in his diet during the three periods and the differences in the amount of exercise taken.

When the investigations were begun, at midnight, November 15, the weight was 120.5 lbs. (54 k. 655 grammes). At the end of the five days it had been reduced to 119.2 lbs. (54 k. 62 grammes). The lightest weight during this period was on the fourth day, when it was 118.5 lbs. (53 k. 745 grammes). On the second day the weight increased to 121.25 lbs. (55 kilos.).

FIRST PERIOD, FIVE DAYS BEFORE THE WALK.—On the first day, the weight being unchanged, Weston walked fifteen miles; he took 122.99 oz. (3,492.17 grammes) of food and drink, containing 361.22 grains (23.404 grammes) of nitrogen. He discharged 44.20 oz. (1,303.08 grammes) in the urine and feces, and 78.79 oz. (2,189.09 grammes) by the lungs and skin. The weather was clear and dry, the temperature ranging between 35° and 46° Fahr. Assuming the usual quantity of food and drink for an ordinary man to be about 90 oz. (2,542 grammes), containing about 310 grains (20 grammes) of nitrogen,* rather an excess was taken on this day. The cutaneous exhalation was excessive. Allowing 20 oz. (567 grammes) for pulmonary exhalation, which is fairly constant, the cutaneous exhalation amounted to 58.70 oz. (1,658.27 grammes), the normal amount being about 30 oz. (850 grammes).†

On the second day there was a diminution in the total quantity of food and drink and in the quantity of nitrogen (total food and drink, 105.43 oz. [2,987.92 grammes]; nitrogen, 288.35 grains [18.682 grammes]), with an increase in weight of 12 oz. (345 grammes), the urine and feces being diminished about 0.5 oz. (15.13 grammes), and the cutaneous exhalation about 29 oz. (834.12 grammes). The weather was a little warmer, but cloudy and damp. The only explanation I can offer for this increase in weight is in the exercise, which was only five miles.

On the third day there was a loss in weight of 20 oz. (567 grammes). On this day there was a further diminu-

* Flint, "Physiology of Man," New York, 1867, vol. ii., Alimentation, p. 124.

† *Id.*, 1866, vol. i., Respiration, p. 447; and, *Id.*, 1870, vol. iii., Secretion, p. 139.

tion in the quantity of food and drink and in the nitrogen (total food and drink, 86.56 oz. [2,453.67 grammes]; nitrogen 272.27 grains [17.641 grammes]). The urine and feces were increased by about 8.25 oz. (243.58 grammes), and the cutaneous exhalation, 4.88 oz. (142.17 grammes). The exercise was five miles, the same as on the second day.

On the fourth day the weight was diminished 24 oz. (687 grammes). The total quantity of food was about the same as on the third day (86.19 oz.—2,443.19 grammes). The nitrogen was increased by about 63 grains (4.065 grammes). The urine and feces were diminished by about 15.5 oz. (455.03 grammes), and the cutaneous exhalation was increased by about 19 oz. (549.55 grammes). The exercise on this day was fifteen miles, which, with the diminished ingesta, will account for the loss in weight.

On the fifth day there was a gain in weight of about 11 oz. (317 grammes). The total quantity of food and drink was increased over the quantity on the fourth day by about 15 oz. (429.44 grammes). The nitrogen was increased by more than 105 grains (6.830 grammes). The urine and feces were about the same as on the fourth day. The cutaneous exhalation was diminished by 22.27 oz. (680.02 grammes). The exercise on this day was only one mile. The increase in weight is to be explained only by the want of exercise and the large quantity of solid food taken.

SECOND PERIOD, FIVE DAYS OF THE WALK.—This period presents the greatest interest as regards the influence of the diet and exercise upon the weight of the body.

On the first day, walking eighty miles and sleeping but one hour, the loss of weight was about 45 oz. (1,224.00 grammes). The quantity of food and drink was increased over the quantity on the day before by about 85 oz. (2,409.75 grammes), the increase being chiefly in liquids. The nitrogen was diminished by 289 grains (18,716 grammes). The feces were but slightly increased. The urine was increased by about 8 oz. (195 cc.). The estimated cutaneous exhalation was increased by 130 oz. (3,723.11 grammes), a little more than two and a half times. The loss in weight was undoubtedly due in a great measure to the extraordi-

nary amount of exercise. I shall endeavor to explain this more fully when I compare the weights for the three periods.

On the second day, walking forty-eight miles and sleeping 4 hours and 28 minutes, there was a further loss of 4 oz. (114 grammes). The quantity of food and drink was diminished by about 21 oz. (582.25 grammes), but the nitrogen was increased by about 114 grains (7.409 grammes). The feces were increased by a little more than 3 oz. (89 grammes). The urine was diminished by about 8.5 oz. (254 cc.). The cutaneous exhalation was diminished by 54 oz. (1,521.38 grammes). The loss of weight I shall endeavor to explain farther on.

On the third day, walking ninety-two miles and sleeping but thirty minutes, the loss of weight was estimated at 20 oz. (567 grammes). The weight was not accurately taken on this day and was averaged.

On the fourth day, walking fifty-seven miles and sleeping one hour, the weight was 36 oz. (1,020.00 grammes) less than on the second day. (This represents the loss for two days.) The food and drink were, for the third day, about 5 oz. (151.09 grammes) more than for the second day, and for the fourth day, about 22 oz. (625.61 grammes) less than for the third day. On the third day the nitrogen was diminished by about 37 grains (2.417 grammes). On the fourth day the nitrogen was further diminished by 84 grains (5.436 grammes). There were no feces on the third day, and the urine was increased by about 7 oz. (209 cc.). On the fourth day the feces were in about average quantity. The urine was diminished about 8 oz. (235 cc.). On the third day the cutaneous exhalation was increased by about 22 oz. (610.82 grammes). On the fourth day the cutaneous exhalation was diminished by about 23 oz. (636.67 grammes). I shall discuss the loss of weight in connection with a comparison of the three periods.

On the fifth day, walking forty and a half miles and sleeping 9 hours and 26 minutes, there was an increase in weight of 28 oz. (793.00 grammes). The food and drink were increased by 36 oz. (1,020.48 grammes). The nitrogen was increased by 239 grains (15.442 grammes), about two and two-thirds times. The feces were diminished by 0.16 oz. (4.50 grammes), and the urine was increased by

about 11 oz. (325 cc.). The cutaneous exhalation was diminished by about 19 oz. (546.61 grammes).

The loss of weight during this period of extraordinary muscular exertion is an interesting question; and it will be considered in connection with, not only the quantities of food, drink, excretions and exhalations, but the quantities of nitrogen introduced and discharged.

THIRD PERIOD, FIVE DAYS AFTER THE WALK.—It is to be remembered that this period was one of nearly absolute repose after the exertion of the preceding five days, with a daily average of eight and a half hours of sleep.

On the first day the weight increased by 36 oz. (1,021.00 grammes). The weight of food and drink was diminished by about 55 oz. (1,662.46 grammes), but the quantity of nitrogen was about the same as on the fifth day of the second period. The feces were diminished by 1.36 oz. (38.50 grammes), and the urine, by about 12 oz. (352.50 cc.). The cutaneous exhalation was diminished by nearly 50 oz. (1,394.50 grammes). The increase in weight was probably due in greatest part to retention of liquids and appropriation of nitrogenous matters to supply the muscular waste that had been going on for the previous five days. For the five days of the walk, for every 100 parts of nitrogen of food there was a discharge of 174.81 parts in the urine and feces. On this, the first day, the discharge of nitrogen was in the proportion of 76.68 parts per 100 parts in the food.

On the second day there was a further gain in weight of 36 oz. (1,021.00 grammes), which brought the weight to 120.25 lbs. (54 k. 539 grammes), about the weight at the beginning of the observations, which was 120.5 lbs. (54 k. 655 grammes). The weight of food and drink was increased by 50.66 oz. (1,436.03 grammes), and the nitrogen was increased by about 113 grains (7.351 grammes). The feces were increased by about 1 oz. (28.35 grammes), and the urine, by about 14.5 oz. (427.15 cc.). The cutaneous exhalation was increased by about 34 oz. (969.41 grammes). This day was warm, clear and dry, the first day being rainy and 5° to 8° Fahr. colder.

On the third day the weight was unchanged. The food and drink were diminished by 59 oz. (1,670.17 grammes), and the nitrogen, by about 104 grains (6.756 grammes).

The feces were increased by 5 oz. (140.5 grammes), a little more than doubled. The urine was increased by 38 oz. (1,125 cc.), nearly doubled. The cutaneous exhalation was diminished by about 66.5 oz. (1,930.61 grammes), more than three times. This day shows a working off by the urine and feces of the unusual amount of food, especially nitrogenous matter, taken on the previous day, the weight remaining stationary.

On the fourth day the weight was increased by 52 oz. (1,474.00 grammes). This great increase is explained by the following circumstance: At 11.15 P. M. Weston took supper, the food and drink weighing 54.75 oz. (1,547.36 grammes). The weight of the body was taken at 11.55 P. M., about the usual hour. This was the only time when anything was eaten after 7.45 P. M. This accident renders it useless to discuss the question of weight on this day. On this day the nitrogen of the food was largely increased, amounting to 641.71 grains (41,578 grammes), the average for an ordinary man being about 310 grains (20 grammes).

On the fifth day the weight was about the same as on the third day, the increase being only 0.5 lb. (226 grammes). On this, the final day of the observations, the weight was about the same as on the first day of the first period, being increased only a quarter of a pound. The food and drink were diminished by about 85 oz. (2,419.09 grammes), and the nitrogen, by about 358.5 grains (23,219 grammes). The feces were increased by about 1 oz. (22.5 grammes), and the urine, by 8 oz. (237 cc.). The cutaneous exhalation was increased by about 1.68 oz. (37.87 grammes).

CAUSES OF THE VARIATIONS IN WEIGHT.*—In a measure, the variations in weight during the fifteen days may be satisfactorily explained; but there are certain questions involved that are as yet obscure. The explanation of the variations during the walk and for the five days after is much facilitated by a comparison of the ingress and egress of nitrogen.

At the beginning of the investigations the weight was 120.5 lbs., which Weston thought was about normal. Dur-

* To avoid complicating the discussion of the causes of the variations in weight, the English weights only will be used.

ing the period of five days before the walk the variations were not very great, the highest being 12 oz. above, and the lowest, 32 oz. below. At the end of the fifth day the weight was reduced by about 21 oz. On the first day, the weight being unchanged, the exercise was fifteen miles. The food was of the usual variety, but its quantity and proportion of nitrogen were about 30 per cent. above the average for an ordinary man. On the second day the diminished exercise, the food being less but still above the normal average, will account for the increase in weight of 12 oz. On the third day the exercise was the same as on the second day; but the food was reduced a little below the normal average, which will account for 20 oz. loss of weight. On the fourth day the food was still below the average, being about the same as on the previous day; but it contained a large proportion of nitrogenous matter, 20 per cent. more than on the third day. The exercise was fifteen miles, which, with the diet, will account for 24 oz. loss of weight. On the fifth day the food was increased to a little above the average, and it contained a large quantity of nitrogen, about 35 per cent. above the average. This fact, with the absolute muscular repose and ten hours' sleep as a preparation for the walk, will readily account for 11 oz. increase in weight. During this period of five days before the walk the average quantity of food and drink was 100.5 oz., containing 339.46 grains of nitrogen, the ordinary average being 90 oz., containing 310 grains of nitrogen. The average discharge of nitrogen by the urine and feces was 95.53 parts per 100 parts of the nitrogen of food, which is about normal. Thus it is evident that the variations in weight during a period of five days of ordinary life can be explained in accordance with generally accepted physiological principles.

In endeavoring to explain the variations in weight that occurred during the walk, and for the succeeding five days, the extraordinary muscular exertion introduces new elements to be considered. These have an important bearing upon the subject of nutrition, disassimilation and "the source of muscular power," about which so much has been written within the last few years.

First: What tissue was consumed, the products being thrown off, during the effort of walking 317½ miles in five

consecutive days? Was it the muscular substance? The importance, as regards the processes of nutrition, of a definite answer to this question can hardly be overestimated.

The loss of weight was undoubtedly due in great measure to the excessive muscular exertion, but in part, also, to change in diet.

The loss must have been either in liquids, fats or muscular substance.

It is not probable that the loss was due in any great degree to a diminution in the proportion of liquids, for the excessive loss from the skin was supplied by liquids taken into the stomach. It is not necessary to cite experiments which show that loss by the skin, as it occurs in hot-air or vapor-baths or in working for an hour or more at a high temperature, is readily compensated by liquid ingesta, as this fact is well settled in physiology.* A glance at the daily tables of food and drink will show that during the five days of the walk Weston took 8 lbs. 8 oz. to 10 lbs. 11 oz. of liquids.

If the loss was due to a consumption of non-nitrogenous matters, it would be chiefly of fat and would be represented by the carbonic acid of expiration. It is certain that the non-nitrogenous constituents of the body do not contribute to the formation of the nitrogenous excrementitious matters.

If the loss was due to a consumption of the nitrogenous constituents of the body, principally of the muscular tissue, this loss, under the extraordinary muscular effort, would be represented by the nitrogen of the excretions. It is not probable that the nitrogenous constituents of the body are in any considerable amount changed into non-nitrogenous matter and exhaled in the form of carbonic acid, though this probably does occur to some extent.

The question then resolves itself to one of the relative consumption and elimination of nitrogenous matters. The following are the facts on this point, observed during the five days of the walk:

During the five days of the walk † Weston consumed in all, 1,173.80 grains (76.055 grammes) of nitrogen in his

* See my work on Physiology, New York, 1870, vol. iii., p. 140 *et seq.*

† I have reduced these calculations, on account of their great importance, to grammes.

food. During the same period he eliminated 1,807.60 grains (116.084 grammes) of nitrogen in the urine and feces. This leaves 633.80 grains (40.030 grammes) of nitrogen, over and above the nitrogen of the food, which must be attributed to the waste of his tissues, and probably almost exclusively to the waste of his muscular tissue. According to the best authorities, lean meat uncooked, or muscular tissue, contains 3 per cent. of nitrogen.* The loss of 633.80 grains (40.030 grammes) of nitrogen would then represent a loss of 21,127.00 grains (1,334.33 grammes), or 3.018 lbs. of muscular tissue. The actual loss of weight was 3.450 lbs. (1,565.00 grammes). This allows about 0.43 lb. (230.67 grammes) loss unaccounted for, which might be fat or water.

The correspondence of these figures of loss calculated from the quantity of nitrogen eliminated with the actual loss in weight leaves little room for doubt in regard to the fact that the immense exertion during this period of five days was attended with consumption of muscular substance. Those who have adopted the view that the muscular system is like a steam-engine, consuming in its work food as fuel and not its own substance, may say that this is an extraordinary case, as it undoubtedly is; but the facts developed by the foregoing observations prove, none the less conclusively, that the muscular system may consume its own substance by exercise, even when the individual takes all the food required by his appetite. It can hardly be, however, that the foregoing facts are not in accordance with a general physiological law.

It will be interesting, now, to study the behavior of the system after the walk, when there was almost absolute repose and when the quantity of nitrogen taken with the food was largely increased. The important question here is the following:

In the return of the weight to the normal standard, did the muscular tissue take up nitrogen to repair the excessive waste engendered by the five days of exertion?

In two days after the walk the weight had increased to within four ounces of the weight at the beginning of the observations, five days before the walk. It is not to be

* Payen, "Précis théorique et pratique des substances alimentaires," Paris, 1865, p. 488.

expected that this increase would be due entirely to appropriation of nitrogenous matter by the muscular system. Reference to the tables of diet for these two days shows that the food taken was about 155 oz. each day, the normal average being assumed at 90 oz., an excess of a little more than 70 per cent. The nitrogen taken was about 50 per cent. in excess of the normal quantity. The tables also show a large proportion of non-nitrogenous matter in the food on those days. The exercise was only two miles daily. Weston gained in weight 4.5 lbs. He retained in his system a quantity of nitrogen equivalent to 1.1 lb. In view of the muscular inactivity and the large proportion of non-nitrogenous matter in the food, it is fair to assume that the remaining 3.4 lbs. were due to accumulation of fat. This, however, is a point incapable of positive demonstration. Taking the entire period of five days after the walk, the gain in weight was five pounds, which brought it to 4 oz. above the weight at the beginning of the fifteen days. The excess of the nitrogen of food over the nitrogen of the urine and feces represented, for these five days, an accumulation of 1.6 lb. of muscular substance. During this time there was almost complete repose of the muscular system. The daily quantity of food was about 61 per cent. over the normal average, and the nitrogen, about 42 per cent. over the average. The food contained, also, a large proportion of non-nitrogenous matter.

These facts seem to indicate that after the effort in walking $317\frac{1}{2}$ miles in five consecutive days, for five days of muscular inactivity, the quantity of food being large and containing a greater proportion of non-nitrogenous matter than the food taken either before or during the walk, the muscular system appropriated 1.6 lb. of nitrogenous matter, and the entire body accumulated about 3.4 lbs. of fat. It is well known that athletes, after a season of severe training by exercise and nitrogenous diet, accumulate fat very rapidly, when the muscles are allowed repose and the diet is unrestricted.

TEMPERATURE, PULSE AND RESPIRATIONS

The temperature under the tongue for every day during the three periods was carefully taken, as nearly as possible at the same hour and under the same conditions. During

the five days of the walk the temperature was taken after the day's walk had been accomplished; and during the five days before and the five days after the walk it was taken generally between 10.45 P. M. and midnight.

FIRST PERIOD, FIVE DAYS BEFORE THE WALK.—The temperatures for each day do not present any great range of variation. The data here are useful chiefly as indicating the normal average under ordinary conditions. The highest temperature was at the end of the first day. It was then 99.7° Fahr. (37.6° C.). The lowest temperature was on the third day, when it was 98° Fahr. (36.7° C.). On the first day the quantity of food and drink and the proportion of nitrogen were above the average by about 20 per cent. The exercise was fifteen miles. On the third day the quantity of food and drink was a very little below the average, and less nitrogen was taken than on any of the five days. The exercise was five miles. On the fifth day the temperature was within 0.2° Fahr. of the temperature on the first day. On this day the quantity of food and drink was slightly above the average, but the nitrogen of the food was increased by 42 per cent. The exercise was only one mile. On the first day the weather was clear, the highest temperature in the shade was 46° and the lowest, 35° Fahr. On the fifth day it also was clear, and the highest temperature was 43° and the lowest, 30° Fahr. On the third day the meteorological record was, "slight rain and slight snow 6.15 P. M.," highest temperature 42°, and lowest 29° Fahr. On the fourth day, when the temperature under the tongue was 99.1° Fahr. (37.3° C.), the external temperature was 36°, highest, and 27°, lowest, "snow-squalls, clear evening." On this day the total quantity of food and drink was the same as on the third day, but the nitrogen of the food was increased by about 23 per cent. On the fourth day the exercise was fifteen miles. On the second day, when the temperature under the tongue was 98.4° Fahr. (36.9° C.), the nitrogen of the food was only 16.08 grains more than on the third day. The weather was cloudy, the highest temperature, 47° and the lowest, 37° Fahr.

In the range of temperature during the five days of this period, there does not seem to be any marked difference due to the exercise. The variations apparently bear some

relation to the quantity of nitrogenous food, the temperature being high when the nitrogen of the food is abundant and low when the proportion is small. The temperature was markedly higher on the clear days, without any definite relation to the external temperature.

The range of temperature for these five days was about normal, 98° to 99.7° Fahr. (36.7° to 37.6° C.). In my work on physiology I have taken, as the standard temperature under the tongue, 98° Fahr., subject to variations within the limits of health of about 0.5° below and 1.5° above.*

The average temperature for the first period of five days before the walk, which I shall take as the standard for comparison with the temperatures at the other periods, is 99° Fahr. (37.2° C.).

SECOND PERIOD, FIVE DAYS OF THE WALK.—The variations in temperature during this period are remarkable, and are highly interesting from their possible physiological relations. By reference to the meteorological table (E.), it will be seen that the weather during this period was generally cloudy, without much variation from day to day in the thermometer. There does not appear to be any constant relation, during this period, between the temperature and the daily consumption of nitrogen.

On the first day, between 12.15 A. M. and 10.32½ P. M. Weston walked eighty miles. His temperature was taken eight minutes after he had completed the walk, and was 95.3° Fahr. (35.3° C.), 4.3° less than the last temperature taken before the walk was begun. This is a large reduction, greater than ever occurs under the ordinary conditions of health; and it can be attributed only to the extraordinary muscular exertion during the day.

On the second day, between 4.58 A. M. and 4.5 P. M., Weston walked forty miles, when he stopped for 6 hours and 19 minutes. At 10 P. M., about six hours after the stop, the temperature was 94.8° Fahr. (34.9° C.), a reduction from the temperature of the first day of 0.5° . Weston did not sleep well, as he had hoped to do during the six hours. At 10.24 P. M. he began his first effort to walk one hundred and twelve miles in twenty-four consecutive hours.

* "Physiology of Man," New York, 1870, vol. iii., Nutrition, p. 396.

I now think the further lowering in the temperature was an indication of want of proper reaction after the walks he had already accomplished. Had I appreciated the facts at that time, I should have advised him to defer his attempt to accomplish the hundred and twelve miles until a later period. As it was, the attempt was a failure.

As on the first day the lowering in temperature is to be attributed only to the excessive and prolonged muscular exertion.

On the third day, between midnight of the second day and 10.52 P. M., Weston walked ninety-two miles. At 11.15 P. M. the temperature was 96.6° Fahr. (35.9° C.), 1.8° higher than on the second day.

On the fourth day Weston walked fifty-seven miles between 1.33 A. M. and 10.30 P. M. The temperature, taken at 10.40 P. M., was 96.6° Fahr. (35.9° C.), the same as on the third day. This was the day on which the walk was interrupted by breaking down.

On the fifth day Weston walked forty and a half miles between 9.56 A. M. and midnight. He continued walking for fifteen minutes after midnight. He was in fine spirits all day. During this twenty-four hours, for the first time, he got sufficient refreshing sleep. He slept nine hours and twenty-six minutes. The temperature, taken at 1.30 A. M. of the next day, was 97.9° Fahr. (36.6° C.); an increase of 1.3° over the temperature of the day before.

It is difficult to explain satisfactorily the elevation of temperature by 1.8° on the third day, the day of the longest walk, and the same temperature on the fourth day, when Weston broke down completely. The temperature, however, on these days was still 2.4° below the average of the five days before the walk, and 2° below the average of the five days after the walk. The elevation in temperature on the fifth day, by 1.3°, was probably on account of the sleep of nine hours and twenty-six minutes.

The average temperature during this period was 96.3° Fahr. (35.7° C.); 2.7° below the average of five days before, and 2.3° below the average of five days after the walk. The nearly uniform depression of temperature during this period of excessive exertion shows pretty conclusively that severe and prolonged muscular exercise diminishes the heat of the body. It has been observed that

during or immediately after moderate exercise, the heat of the body is increased; and that the actual temperature of the muscles is sensibly elevated; * but this is quite different from the great muscular and nervous strain to which Weston subjected himself for five days. The fact of diminution of temperature during this period remains, therefore, without any explanation, except that it was probably due to some unusual condition of the nervous system.

THIRD PERIOD, FIVE DAYS AFTER THE WALK.—During this period there was but little variation in the temperature from day to day. On the first day the temperature was 98.6° Fahr. (37° C.), 0.7° higher than on the last day of the walk. This temperature was about normal. On the second day the temperature was 98.4° Fahr. (36.9° C.); on the third day, 99.3° Fahr. (37.4° C.); on the fourth day, 98.8° Fahr. (37.1° C.); and on the fifth day, 97.5° Fahr. (36.4° C.). This range of temperature was about normal, assuming, as I have done, that the average is 98° Fahr., with a range of 0.5° below and 1.5° above. The average temperature for the five days was 98.6° Fahr. (37° C.), 0.4° less than the average for the five days before the walk and 2.3° more than the average for the five days of the walk.

In studying the variations in temperature from day to day during this period, I have not been able to find any definite relation with the food or with the meteorological record. The difference between the average during this period and the average for the five days before the walk is insignificant. It is interesting to note, however, that so soon as the extraordinary muscular effort ceased, the temperature returned to about the normal standard.

PULSE AND RESPIRATIONS.—During the first period there was very little variation in either the pulse or respirations. The extremes for the pulse were 93 and 71. The pulse was 93 just before the walk; and this probably was due to excitement incident to the occasion. At that time, also, the respirations were 25. For the first three days the respirations were 20, and on the fourth day, 23.

* For an account of different observations on this point, see my work on *Physiology*, New York, 1870, vol. iii., *Nutrition*, p. 413.

During the five days of the walk the pulse ranged between 68 and 109. The pulse was 109 on the third day, when the exercise was ninety-two miles. The range of the respirations was between 18 and 23. On the fourth day, after Weston had completely broken down in his walk, the pulse was 68 and the respirations 18.

For the five after the walk the range of the pulse was between 70 and 78, and the respirations were between 22 and 24.

The averages for the five days before the walk were, for the pulse, 78, respirations 22; for the five days of the walk, pulse 90, respirations 21; and for the five days after the walk, pulse 74, respirations 23.

In the absence of sphygmographic records of the pulse, there could be little learned from the observations on the circulation. The variations in the respirations, also, convey little information. It was impossible, however, to make the records on these points more elaborate; and as it was necessary to make all of the observations without subjecting Weston to any considerable annoyance or loss of time, experiments with the sphygmograph would have been impracticable.

The records in regard to sleep, exercise, quantity of food and drink and the composition of the food were made to be used in connection with the question of the elimination of nitrogen, and will not, therefore, be discussed separately. The cutaneous and pulmonary exhalations were calculated from the weight of ingesta, urine and feces and the variations in the weight of the body. As these were not directly estimated they will not be discussed under distinct heads.

VARIATIONS IN THE URINE DUE TO EXERCISE, STUDIED IN CONNECTION WITH THE PROPORTION OF NITROGEN IN THE FOOD

In discussing the variations in the urine during the three periods into which the investigations were divided, I shall take up first the quantity; then the urea, or the quantity of nitrogen eliminated in the urea, in connection with the nitrogen of the feces, and compare the total elimination of nitrogen with the quantity introduced with the food;

then the uric acid and its relations to the urea; and finally, the inorganic salts and abnormal matters.

QUANTITY OF URINE

The most important point to determine in this connection is whether the immense amount of exercise during the five days of the walk had any influence on the elimination of water by the kidneys. This can be settled with tolerable accuracy, inasmuch as the liquids taken each day were carefully measured.

FIRST PERIOD, FIVE DAYS BEFORE THE WALK.—The range of variation in the quantity of urine during this period was not great, the extremes being 32.45 fl ℥ (960 cc.) and 46.15 fl ℥ (1,365 cc.). The variations do not present any definite relation to the quantity of liquids. On the fourth day, with 32.45 fl ℥ of urine, the liquids taken amounted to 68.73 fl ℥. On the third day, with 46.15 fl ℥ of urine, the liquids taken amounted to 55.56 fl ℥. On the third day, when the quantity of urine was the greatest, the meteorological record is the following: Thermometer, highest, 42° Fahr., lowest, 29° Fahr.; humidity (saturation 100) 61.36; "slight rain and slight snow at 6.15 P. M." The humidity on that day was the greatest of the five. On the fourth day, when the quantity of urine was the least, the record was as follows: Thermometer, highest, 36° Fahr., lowest, 27° Fahr.; humidity 56.66; "snow-squalls, clear evening." During this period the excess of liquids taken must have been discharged through the skin.

The average quantity of urine during these five days was 37.84 fl ℥ (1,134 cc.). The average quantity of liquids taken daily was 65.56 fl ℥ (1,966.8 cc.).

SECOND PERIOD, FIVE DAYS OF THE WALK.—The range of variation in the quantity of urine during this period also was slight, the extremes being 43.60 fl ℥ (1,290 cc.), on the fifth day, and 32.52 fl ℥ (965 cc.), on the fourth day. The variations bore no definite relation to the meteorological record. On the day of greatest discharge of urine, the liquids taken amounted to 151.06 fl ℥. On the day of the least urine, the liquids taken amounted to 137.04 fl ℥. During this period the relations between

the quantity of urine and of liquids taken were pretty constant: first day, urine, 42.09 fl 3; liquids taken, 171.67 fl 3; second day, urine, 33.50 fl 3; liquids taken, 136.40 fl 3; third day, urine, 40.56 fl 3; liquids taken, 158.75 fl 3; fourth day, urine, 32.52 fl 3; liquids taken, 137.04 fl 3; fifth day, urine, 43.60 fl 3; liquids taken, 151.06 fl 3.

The average quantity of urine during these five days was 38.46 fl 3 (1,138 cc.). The average quantity of liquids taken was 150.40 fl 3 (4,512 cc.).

The average of 38.46 fl 3 (1,138 cc.) for the five days of the walk, against 38.14 fl 3 (1,134 cc.), for the five days before the walk, shows that the walk of 317½ miles in five days did not affect the quantity of urine, and that the large quantities of liquids taken during that time must have been discharged by the skin.

THIRD PERIOD, FIVE DAYS AFTER THE WALK.—The variations in the daily discharge of urine during this period were very considerable, the extremes being 84.18 fl 3 (2,490 cc.), on the third day, and 31.59 fl 3 (937.5 cc.), on the first day. The variations bore no definite relation to the meteorological record. There was no definite relation between the quantity of urine and the liquid ingesta. On the third day, with 84.18 fl 3 of urine, the liquids taken amounted to 57.87 fl 3; and on the first day, with 31.59 fl 3 of urine, the liquids taken amounted to 46.74 fl 3. On the second day the liquids taken amounted to 104.82 fl 3, and the urine discharged, 46.14 fl 3.

The average quantity of urine during these five days was 58.14 fl 3 (1,720 cc.). The average quantity of liquids taken was 69.22 fl 3 (2,076 cc.).

During the five days after the walk, for every 100 parts of liquid ingesta the kidneys discharged 84 parts. During the five days before the walk, for every 100 parts of liquid ingesta the kidneys discharged 58 parts. This is probably to be explained by the exercise of 8.2 miles daily for the five days before the walk, which would increase the action of the skin, while after the walk the exercise was only 2.2 miles daily.

It will not be necessary to consider under a separate head the variations in the specific gravity of the urine, as this simply represents the solid constituents, which will be taken up separately.

INFLUENCE OF EXERCISE UPON THE ELIMINATION OF NITROGEN, CHIEFLY IN THE UREA, AND THE RELATIONS BETWEEN THE NITROGEN DISCHARGED AND THE NITROGEN INGESTED

As regards the elimination of nitrogen, the investigations were undertaken chiefly with reference to the influence of the great muscular exertion during the five days of the walk. In order to ascertain exactly the quantity of nitrogen excreted at this time as compared with that discharged under ordinary conditions, the nitrogen of both the urea and feces was taken. The proportion of nitrogen in the uric acid, creatin and creatinin of the urine is so insignificant, as compared with the total discharge, that it would hardly modify the results of the calculations. During the fifteen days Weston took food according to his fancy. At certain times during the walk he took large quantities of tea and coffee; but the results of the calculations show that the modifications, if any, in the discharge of urea produced by these articles must have been greatly overshadowed by those due to the muscular exercise. In the discussion of this, the most important of the questions involved, the influence of food will be treated of from a secondary point of view. As regards this point there is no difference of opinion. Nitrogenous food always increases the elimination of urea; and so marked is this, that many physiologists hold the view that urea is derived almost entirely from the food. This is one of the physiological questions settled by these observations.

From the foregoing considerations it is evident that the only accurate way to determine the modifications in the elimination of nitrogen that are to be attributed to muscular exercise, is to calculate for each period, and for every day of each period, the proportion borne by the nitrogen in the urea and feces to the nitrogen of the food. It is true that the influence of the food of one day may be prolonged for one or more days, and the same remark may possibly apply to the exercise; but the periods of five days each are sufficiently long to obviate any serious error from this cause. I have learned, however, from these calculations, that a period much shorter would not be entirely satisfactory.

The conclusions that I shall arrive at will all be drawn from Tables A.¹ B.¹ C.¹ for the first period; Tables A.² B.² C.² for the second period; and Tables A.³ B.³ C.³ for the third period. Table D. gives the daily averages for the three periods.

FIRST PERIOD, FIVE DAYS BEFORE THE WALK.—For the first day of this period the total nitrogen of the urea and feces was 323.26 grains (20.945 grammes). The nitrogen of the food was 361.22 grains (23.404 grammes). For every 100 parts of nitrogen of food, there were discharged in the urea and feces, 89.49 parts. The exercise was fifteen miles. The nitrogen of the food was about 30 per cent. above the average for an ordinary man. The elimination of nitrogen per 100 parts of the nitrogen of food was considerably below the average.

On the second day the total nitrogen of the urea and feces was 301.18 grains (18.181 grammes). The nitrogen of the food was 288.35 grains (18.682 grammes). For every 100 parts of nitrogen of food, there were discharged in the urea and feces, 104.45 parts. The exercise was five miles. The nitrogen of the food of this day was a little below the average.

On the third day the total nitrogen of the urea and feces was 330.36 grains (21.405 grammes). The nitrogen of the food was 272.27 grains (17.641 grammes), much below the average for an ordinary man, which I put at 310 grains. For every 100 parts of nitrogen of food, there were discharged in the urea and feces, 121.3 parts. The exercise was five miles.

On the fourth day the total nitrogen of the urea and feces was 300.57 grains (19.475 grammes). The nitrogen in the food was 335.01 grains (21.706 grammes), a little above the average for an ordinary man. For every 100 parts of nitrogen of food, there were discharged in the urea and feces, 89.75 parts. The exercise was fifteen miles.

On the fifth day the total nitrogen of the urea and feces was 320.06 grains (20.737 grammes). The nitrogen of the food was 440.43 grains (28.536 grammes), much above the average. For every 100 parts of nitrogen of food, there were excreted in the urea and feces, 72.67 parts. The exercise was one mile, with ten hours' sleep.

Taking the averages for the five days, the nitrogen of the urea and feces daily was 315.09 grains (20.149 grammes). The daily nitrogen of the food was 339.46 grains (21.994 grammes). For every 100 parts of nitrogen of food, there were excreted in the urea and feces, 92.82 parts, which may be taken as about the normal average under ordinary conditions.

From these figures, the following conclusions may be drawn:

I. Under ordinary conditions about 93 per cent of the nitrogen of food is represented in the urea and feces; and the remaining 7 per cent. may be put down to nitrogen discharged in other ways and to an allowance for error in the estimates, particularly in the food.

II. In view of the unusual power of endurance of Weston and his habit of walking long distances, I do not think that the variations in the exercise during the five days are to be regarded as sufficient to influence, to any great extent, the elimination of nitrogen; and I consider that these variations are due chiefly to the nitrogen of the ingesta. The influence of the food probably is manifested in a more marked manner one or two days after than on the day on which the excess of nitrogen is taken. This fact has been recognized by physiologists, especially since the researches of Lehmann, to which reference has already been made.* On the first day there was about 30 per cent. of excess of nitrogen of the food, and 89.49 parts of nitrogen discharged per 100 parts of nitrogen taken in. On the second and third days the nitrogen of the food was a little below the average. On these days there was an average of 111.65 parts of nitrogen discharged per 100 parts of nitrogen taken in. On the fourth day the nitrogen of the food was slightly in excess, with 89.75 parts per 100 discharged. On the fifth day the nitrogen in the food was very largely in excess (42 per cent.), with 72.67 parts per 100 discharged. The absolute quantity of nitrogen discharged on the fifth day was large, but the proportion per 100 of the nitrogen of food was overbalanced by the large quantity introduced.

What is the mechanism of the influence of nitrogenous

* Lehmann, "Physiological Chemistry," Philadelphia, 1855, vol. i., p. 150.

food upon the discharge of nitrogen by the excretions? Does the excremental nitrogen come from a direct change of the nitrogenous constituents of the blood into urea in the blood itself, or is it derived from the nitrogenous food used, through the blood, in building up the nitrogenous semisolids of the body, passing into the excretions through the processes of nutrition and disassimilation?

Although the answers to these questions are perhaps beyond the limits of actual demonstration, the attainable facts point very strongly to the following:

The nitrogenous food occupies several hours in its digestion and its appropriation by the blood, where it is changed into the nitrogenous nutritive constituents of the circulating fluid. The process of its appropriation by the nitrogenous constituents of the tissues, particularly in the muscular system, is probably slower still. The chief product of disassimilation of the nitrogenous constituents of the tissues is urea; and its separation is very slow and gradual. This fact is illustrated by the slow accumulation of urea in the blood after extirpation of the kidneys. If this is the mechanism of the production of urea, the increase in its quantity would be marked for a day or two after the introduction of an excess of nitrogenous food; and this is a fact demonstrated by actual observation. If the excess of urea were directly formed in the blood from an excess of nitrogenous food, being discharged by the urine and leaving a stated and but slightly variable quantity resulting from the actual disassimilation of the tissues, its increased discharge from an excess of nitrogenous food would be more rapidly developed.

SECOND PERIOD, FIVE DAYS OF THE WALK.—On the first day of this period Weston walked eighty miles, with one hour of sleep. The total nitrogen of the urea and feces was 357.10 grains (22.167 grammes). The nitrogen of the food was reduced more than 50 per cent. below the average, being only 151.55 grains (9.820 grammes). For every 100 parts of nitrogen introduced there were 235.63 parts of nitrogen discharged.

This very great discharge of nitrogen in proportion to the nitrogen of the food may be in part explained by the large excess of nitrogen taken the day before; but by far the greatest part can be attributed only to the extraordi-

nary muscular exertion and the consequent waste of muscular tissue. The loss of weight on the first day was 43.2 oz. (1,224.00 grammes).

On the second day Weston walked forty-eight miles, with 4 hours and 28 minutes of sleep. The total nitrogen of the urea and feces was 370.64 grains (24.015 grammes). The nitrogen of the food was largely increased, being 265.92 grains (17.229 grammes). For every 100 parts of nitrogen introduced, there were discharged, 139.39 parts. On this day there was still a large excess of nitrogen discharged; but the proportion per 100 parts of the nitrogen introduced was reduced by the increase in the proportion in the food. The excessive discharge of nitrogen on this day is to be attributed almost exclusively to the muscular exertion of that, and, perhaps, of the previous day.

On the third day Weston walked ninety-two miles, with 30 minutes of sleep. The entire quantity of nitrogen of the urea (no feces were passed) was very large, amounting to 397.58 grains (25.760 grammes), representing 851.95 grains (55.200 grammes) of urea, by far the largest quantity discharged in any one of the five days. This corresponded to the greatest amount of muscular exertion, a fact which is very significant. The nitrogen of the food was slightly diminished, amounting to 228.61 grains (14.812 grammes). For every 100 parts of nitrogen introduced, there were discharged, 173.91 parts. This excessive discharge of nitrogen can be attributed only to the muscular exertion. On that day Weston took six pints of strong coffee, which, if it had any effect, would have diminished the elimination of urea.

On the fourth day Weston walked fifty-seven miles, with one hour of sleep. The nitrogen of the urea and feces was 348.53 grains (22.582 grammes). The nitrogen of the food was on this day diminished to the minimum, being only 144.70 grains (9.376 grammes). For every 100 parts of nitrogen introduced, there were discharged, 240.86 parts, the largest excess observed during the five days.

At 10.30 P. M., on this day, Weston broke down completely. He could not see the track and was taken staggering to his room, having reached apparently the limit of his endurance. His condition at that time, as shown by the records, was as follows: He had lost in weight 83.2

oz. (2,358.00 grammes), being reduced from 119.2 lbs. (54 k. 62 grammes) to 114 lbs. (51 k. 704 grammes). He had taken a daily average of 197.70 grains (12.809 grammes) of nitrogen in his food, while walking an average of sixty-nine and a quarter miles per day, with an average of sleep in each twenty-four hours of 1 hour and 44 minutes, for four days. His daily average of nitrogen should have been 310 grains (about 20 grammes), not allowing for an increased quantity demanded to supply the waste engendered by his excessive muscular exertion. He had discharged for every 100 parts of nitrogen introduced, a daily average of 186.37 parts for four days. The calculations, as well as the general condition of the system, show that the period had probably arrived when repair of the muscular tissue had become absolutely necessary.

If these facts are to be accepted—and leaving the widest margin for inaccuracy in the estimates, they can not involve any considerable error—it is difficult to come to any other conclusion than that excessive and prolonged muscular exercise increases largely the excretion of nitrogen, and that the excess of nitrogen discharged is due to an increased disassimilation of the muscular substance; and it is to be remembered that the experiments upon which this statement is based were made with a diet regulated entirely by the wishes of the person under observation.

On the fifth day, after 9 hours and 26 minutes of sleep, the system reacted completely, and Weston walked forty and a half miles. The nitrogen of the urea and feces was 332.77 grains (21.561 grammes). The nitrogen of the food was increased 165 per cent., being 383.04 grains (24.818 grammes). For every 100 parts of nitrogen of food, there were discharged, 84.27 parts. The absolute quantity of nitrogen discharged was still very great; but the proportion to the nitrogen introduced was reduced by the large quantity in the food.

On this day, when there was apparent reaction after the complete prostration of the fourth day, the system seemed to appropriate nitrogen with avidity, to repair the impoverished muscular tissue. The weight was increased on this day by 28 oz. (793 grammes).

A study of the averages for the five days of this period develops points of much importance, some of which have

already been considered in connection with the variations in weight:

I. The absolute discharge of nitrogen by the urea and feces for each day, without considering the nitrogen of the food, is in a nearly uniform proportion to the number of miles walked. This proportion is but little disturbed if it is assumed that the influence of the ingestion of nitrogen is prolonged for a period of twenty-four to forty-eight hours.

II. During the walk of $317\frac{1}{2}$ miles in five consecutive days, for every 100 parts of nitrogen taken in with the food, there were discharged in the urea and feces, 153.99 parts, against 92.82 parts per 100 for the five days before the walk, and 84.63 parts per 100 for the five days after the walk.

III. The actual loss of weight during the five days of the walk, was 3.45 lbs. (1,565.00 grammes). The total quantity of nitrogen discharged in the urea and feces during this period, in excess of the nitrogen taken in with the food, was 633.80 grains (40.030 grammes). Assuming that 3 parts of this nitrogen represent the waste of 100 parts of muscular tissue, the loss of muscular tissue calculated from the nitrogen excreted would be 3.018 lbs. (1,334.33 grammes), leaving only 0.43 of a pound (230.67 grammes) unaccounted for, which might be fat or water.*

THIRD PERIOD, FIVE DAYS AFTER THE WALK.—The record of the fifth day of the second period shows that the system had already begun to recuperate after the depression of the fourth day, notwithstanding the walk of forty and a half miles. The explanation of this is to be found in the long sleep and the quantity of nitrogenous food taken. During the third period the exercise was practically nothing, being only 2.2 miles daily; the sleep averaged 8 hours and 29 minutes; and the nitrogen of the food averaged 440.93 grains (28.569 grammes). Weston did nothing but eat, sleep and amuse himself, and this was a period of complete bodily and mental repose, very favorable to recuperation after the muscular exertion of the five days before. At the end of the five days the weight had increased to 120.75 lbs. (54 k. 765 grammes), 0.25 of a pound

* See the section on variations in weight.

(110.00 grammes) above the weight at the beginning of the observations. Immediately after the walk Weston felt perfectly well and continued well for the five days, with the exception of a slight headache on the afternoon and evening of the fifth day. He smoked five to seven cigars daily, but took no alcoholic stimulants. His diet was normal in variety, but on some days the quantity of solid food was very large.

On the first day the nitrogen of the food was 385.65 grains (24.987 grammes), about 64 per cent. above the average for the five days of the walk. The nitrogen of the urea and feces was 295.70 grains (19.159 grammes), about 18 per cent. below the average for the five days of the walk. This reduction in the amount of nitrogen excreted is significant. For every 100 parts of nitrogen of food, there were discharged in the urea and feces, 76.68 parts.

On the second day the nitrogen of the food was much increased, being 499.10 grains (32.338 grammes). The nitrogen of the urea and feces was 358.81 grains (23.248 grammes). For every 100 parts of nitrogen of food, there were discharged, 71.81 parts.

On the third day the nitrogen of the food was diminished, though it still largely exceeded the standard for a man under ordinary conditions. On this day it was 394.83 grains (25.582 grammes). The nitrogen of the urea and feces was largely increased, being 409.87 grains (26.556 grammes). For every 100 parts of nitrogen of food, there were discharged, 103.81 parts. This excess of nitrogen discharged is to be attributed to the large quantity of nitrogen taken with the food on the day before.

On the fourth day the nitrogen of the food was in very large quantity, being 641.71 grains (41.578 grammes), more than double the average for a man under ordinary conditions. The nitrogen discharged in the urea and feces was 382.89 grains (24.808 grammes). For every 100 parts of nitrogen of food, there were discharged, 59.67 parts. This proportion was reduced by the very large quantity of nitrogen taken with the food.

On the fifth day the nitrogen of the food was reduced to a little below the average for a man under ordinary conditions, being 283.35 grains (18.359 grammes). The nitrogen of the urea and feces was 418.49 grains (27.125

grammes), much more than the discharge on any other day of the fifteen. For every 100 parts of nitrogen of food, there were discharged, 147.69 parts. This active discharge of nitrogen is explained by the large amount taken in the food on the previous day. On this day, at midnight, the observations were ended.

The daily observations during this period, taken in connection with those during the five days before the walk, seem to establish the following with relation to the influence of nitrogenous food on the excretion of nitrogen:

Every day that an excess of nitrogenous food was taken, it was followed, on the succeeding day, and on one occasion on the succeeding two days, by a largely increased discharge of nitrogen in the urea and feces, the discharge on these days exceeding the amount taken in the food; but the general average for five days, during the period of five days before the walk and the period of five days after the walk, was 85 to 93 parts of nitrogen discharged, for every 100 parts of nitrogen introduced.

The average for the five days after the walk shows an introduction of 440.93 grains (28.569 grammes) of nitrogen daily, an excess of about 42 per cent. over the average for a man under ordinary conditions. For every 100 parts of nitrogen in the food, the average daily excretion, during this period, was 84.63 parts.

INFLUENCE OF EXERCISE UPON THE ELIMINATION OF URIC ACID

The results of the observations during the three periods, as regards the influence of the exercise during the five days of the walk and the influence of food during the five days before and the five days after the walk, are unsatisfactory and are interesting chiefly from a negative point of view.

The quantities of uric acid for each day present very wide variations. For example, on the fourth day of the walk, the exercise being fifty-seven miles, the quantity was 9.21 grains (0.597 of a gramme), the greatest amount for any one day; and on the second day of the walk, the exercise being forty-eight miles, the uric acid was 0.14 of a grain (0.009 of a gramme); the smallest amount for any one

day. On the second day of the first period the quantity was 4.03 grains (0.261 of a gramme); and on the third day after the walk the quantity was 0.31 of a grain (0.02 of a gramme). I have carefully compared the quantities for each day with the exercise and can find no definite relation between them. I have also carefully compared the quantities for each day with the character and quantity of food, but with no more satisfactory result. Inasmuch as on certain days during the walk Weston took large quantities of coffee, it occurred to me that this might influence the uric acid; but I did not find any confirmation of this in the tables. I calculated also for each day the proportion of uric acid per 100 parts of urea discharged, with the view of confirming or disproving the idea that uric acid represents urea in an imperfect condition of oxidation; but the results of these calculations were also unsatisfactory. Finally I compared the sleep and the meteorological record with the uric acid and could establish no relation between them. The variations were so irregular that it was impossible to trace any influence upon the uric acid due to food or exercise, even if it is assumed that the influence might be protracted for a period of one or more days.

As it is impossible to draw any positive conclusions from a comparison of the quantities of uric acid excreted day by day, I can only refer to the averages for the three periods of five days each.

The average daily excretion of uric acid for the five days before the walk was 2.26 grains (0.127 of a gramme). The proportion of uric acid per 100 parts of urea for this period was 0.360 of a part.

The average daily excretion for the five days, walking in all $317\frac{1}{2}$ miles, was 3 grains (0.194 of a gramme). The proportion of uric acid per 100 parts of urea for this period was 0.415 of a part.

The average daily excretion for the five days, walking walk was 1.42 grains (0.082 of a gramme). The proportion of uric acid per 100 parts of urea for this period was 0.195 of a part.

These results, in view of the unexplained daily variations in the uric acid, are not sufficiently definite to lead to any positive conclusions. So far as they go, they show an increase in the uric acid of about 33 per cent. during

the period of extraordinary muscular exertion. During the period of complete muscular inactivity, with an excess of food, the excretion was diminished by about one-half.

The observations have developed, however, the following negative facts:

I. There was no apparent relation between the increase of urea and of uric acid, except that both were increased, with the other solid constituents of the urine. In other words, in increasing the urea by exercise, there is no evidence that uric acid is oxidized and converted into urea; for if that had been the case, with the increase in the quantity of urea, there would have been a diminution in the proportion of uric acid per 100 parts of urea; and this did not occur.

II. It was not shown that the quantity of nitrogenous food has any influence upon the elimination of uric acid; unless it be assumed that the diminution in the uric acid, during the period of inactivity and excess of nitrogenous food, was due to the food alone.

The important physiological results which I hoped to arrive at by studying the uric acid, with the applications of such results to pathological conditions, were not realized; and it must be admitted that positive knowledge of the relations of uric acid to nutrition and disassimilation has not been advanced by these researches, although some important negative facts have been developed.

INFLUENCE OF EXERCISE UPON THE ELIMINATION OF INORGANIC SALTS BY THE KIDNEYS

In studying the variations in the proportions of inorganic salts in the urine, it will be seen that the phosphoric and the sulphuric acid are generally in about the same ratio to each other, their excretion being apparently increased and diminished by the same causes. With the chloride of sodium, however, it is different. For example, on the third day of the walk the quantity of phosphoric acid was large, while the chloride of sodium was in very small quantity, nearly at the minimum. As it is not improbable that different causes may influence, on the one hand, the phosphoric and the sulphuric acid, and on the other, the chloride of sodium, it will be proper to consider the chloride by itself.

PHOSPHORIC AND SULPHURIC ACID.—It is undoubtedly true that the excretion of the phosphates and sulphates by the kidneys is largely influenced by the quantity of these salts in the food. They must, however, pass into the urine in one or both of two ways; either directly from the blood, the salts being taken up by absorption without becoming a part of the tissues, or they may come from the tissues, by a process analogous to that of the production of urea. If these salts passed directly from the blood, their elimination would be almost entirely under the influence of the food; and this influence would be apparent soon after their introduction. If the phosphates and sulphates of the urine are derived from the tissues in the process of disassimilation, when this process is increased in activity, as it was during the five days of the walk, the influence of the food would probably be overshadowed by the exaggerated activity of disassimilation, due to the extraordinary muscular work. It is not possible to subject these questions to rigidly scientific inquiry without estimating exactly the phosphoric and the sulphuric acid in the food. This was impracticable; but the solid food was so little changed in its character during the different days of the three periods, that the variations in its quantity will be to a certain extent a measure of the introduction of the inorganic salts.

FIRST PERIOD, FIVE DAYS BEFORE THE WALK.—During this period the range of variation from day to day was between 43.01 and 67.00 for the phosphoric acid, and between 38.18 and 51.50 for the sulphuric acid. With one exception, these two acids varied from day to day in about the same ratio. On the first day the phosphoric acid was in large quantity, with a small quantity of sulphuric acid. With the exception of the fifth day both the phosphoric and the sulphuric acid were varied in a nearly constant ratio to the variations in the nitrogenous food, being increased with the food and *vice versâ*. On the fifth day, when the quantity of nitrogenous food was the greatest, both the phosphoric and the sulphuric acid were below the average for the five days. On this day the exercise was very little, only one mile.

The most marked and constant variations during this period were with the exercise, especially in the phosphoric acid. On the first day the exercise was fifteen miles; the

phosphoric acid was 51.46 grains (3.334 grammes), the average for the five days being 50.14 grains (3.262 grammes), and the sulphuric acid was 38.37 grains (2.486 grammes), the average being 41.57 grains (2.693 grammes). On the fourth day the exercise was fifteen miles; the phosphoric acid was 67 grains (4.341 grammes), and the sulphuric acid, 51.50 grains (3.337 grammes). On this day the loss of weight was 24 oz. (687 grammes), the greatest loss for any one of the five days. On the second and third days both the phosphoric and the sulphuric acid were slightly below the average for the five days, with five miles of exercise each day. On the fifth day, with ten hours of sleep and one mile of exercise, the phosphoric acid was 43.01 grains (2.787 grammes), and the sulphuric acid, 38.18 grains (2.474 grammes), the smallest quantities during the five days.

During this period the increase in the phosphoric and the sulphuric acid with the exercise was constant.

SECOND PERIOD, FIVE DAYS OF THE WALK.—During this period the ratio of variations between the phosphoric and the sulphuric acid was constant, with the exception of the fifth day, when the quantity of sulphuric acid was a little greater than on the fourth day, while the phosphoric acid was less. During this period there was no definite relation between the quantities of these two acids and the nitrogenous food; the influence of the food being apparently overshadowed by the exercise. The relations between the phosphoric acid and the exercise were nearly absolute. Taking the exercise from the highest to the lowest points, the relations were as follows:

Third day.	Exercise	92 miles.	H_2PO_4	102.25 grains (6.625 grammes).
First day.	"	80 "	"	84.95 " (5.504 ").
Fourth day.	"	57 "	"	66.90 " (4.296 ").
Second day.	"	48 "	"	72.14 " (4.674 ").
Fifth day.	"	40½ "	"	57.49 " (3.725 ").

The variations in the sulphuric acid were not so regular:

Third day.	Exercise	92 miles.	H_2SO_4	63.71 grains (4.128 grammes).
First day.	"	80 "	"	73.39 " (4.755 ").
Fourth day.	"	57 "	"	32.66 " (2.116 ").
Second day.	"	48 "	"	56.90 " (3.687 ").
Fifth day.	"	40½ "	"	40.84 " (2.646 ").

These calculations show a decided and nearly absolute relation between the excretion of phosphoric acid and the

exercise. On the fourth day, with fifty-seven miles of exercise, the nitrogen of the food was about forty-six per cent. less than on the second day, with forty-eight miles of exercise. This will perhaps account for the diminished excretion during the day of less exercise.

As regards sulphuric acid, the conclusions are about the same as for phosphoric acid. The diminished excretion on the second day is also accounted for by the small quantity of nitrogenous food taken on that day.

THIRD PERIOD, FIVE DAYS AFTER THE WALK.—During this period the exercise was practically nothing; and this element does not, therefore, enter into the calculation of the variations of the inorganic constituents of the urine. Although the variations in the phosphoric and the sulphuric acid were considerable, as were the daily variations in the nitrogenous food, there seemed to be no definite relation between them. I shall therefore give for this period simply the extremes and the averages.

On the third day the quantities both of phosphoric and of sulphuric acid were the greatest. The phosphoric acid was 105.68 grains (6.847 grammes). The sulphuric acid was 53.57 grains (3.471 grammes). On the first day the phosphoric acid was least in quantity, being 29.06 grains (1.833 grammes), with 49.53 grains (3.209 grammes) of sulphuric acid. On the second day the sulphuric acid was least in quantity, being 46.07 grains (2.985 grammes), with 46.93 grains (3.041 grammes) of phosphoric acid.

The averages for the five days of this period were as follows: Phosphoric acid, 56.89 grains (3.674 grammes); sulphuric acid, 49.02 grains (3.176 grammes).

AVERAGES FOR THE THREE PERIODS.—The averages for the three periods of five days each show the influence of exercise upon the elimination of phosphoric and sulphuric acid; and the averages for the period of five days before the walk and the period of five days after the walk show the influence of food, probably attributable to the phosphates and sulphates combined with the nitrogenous matters.

For the first period, five days before the walk, the average discharge of phosphoric acid was 50.14 grains (3.262 grammes), and of sulphuric acid, 41.57 grains (2.693

grammes). The average quantity of nitrogen in the food was 339.46 grains (21.994 grammes).

For the second period, five days of the walk, the average discharge of phosphoric acid was 76.63 grains (4.965 grammes), and of sulphuric acid, 53.50 grains (3.666 grammes). The average quantity of nitrogen in the food was 234.76 grains (13.211 grammes).

For the third period, five days after the walk, the average discharge of phosphoric acid was 56.89 grains (3.674 grammes), and of sulphuric acid, 49.02 grains (3.176 grammes). The average quantity of nitrogen in the food was 440.93 grains (28.569 grammes).

These averages show that the walk of $317\frac{1}{2}$ miles in five consecutive days increased the excretion of phosphoric acid more than 50 per cent. over the excretion under ordinary conditions, notwithstanding that the nitrogenous food was diminished 31 per cent. Under the same conditions there was an increase of about 30 per cent. in the excretion of sulphuric acid. The influence of exercise upon the excretion of the phosphates and sulphates, irrespective of the composition of the food, can hardly be doubted.

A comparison of the averages for the first period, five days before the walk, and the third period, five days after the walk, shows an increase in the excretion of phosphoric acid, for the third period, of 13.4 per cent., with an increase of 30 per cent. in the quantity of nitrogenous food. Under the same conditions the excretion of sulphuric acid was increased by 19.2 per cent.

CHLORIDE OF SODIUM.—In the absence of exact estimates of the quantities of chloride of sodium contained in the food of each day, there is little to be learned from the variations in excretion of this salt by the kidneys. Such estimates were manifestly impracticable. The salt used as a condiment was averaged for the four days of the first period and for the fifth day of this period, with the five days of the walk. For the five days after the walk the quantity of salt used was weighed each day. I can form no definite idea of the salt used in cooking for the five days before the walk and the five days after the walk; but on some of the days of the walk, particularly the third and fourth, the diet consisted largely of beef-essence and oat-meal-gruel. No salt was added to the beef-essence, which

was prepared under my own direction, and very little was used in the preparation of the oatmeal-gruel.

FIRST PERIOD, FIVE DAYS BEFORE THE WALK.—The average quantity of salt used as a condiment during this period was 34.5 grains (2.235 grammes). During the five days the proportion of nitrogenous food and the elimination of chloride of sodium presented no definite relation to each other. The variations in the chloride of sodium of the urine were not considerable and had no definite relation to the exercise. The greatest quantity was on the first day, being 195.02 grains (12.636 grammes); and the smallest quantity was on the fourth day, when it was 106.68 grains (6.912 grammes). In the absence of any definite relation between the excretion of chloride of sodium and either the food or the exercise, I can use only the average for this period, which was 159.45 grains (10.331 grammes).

SECOND PERIOD, FIVE DAYS OF THE WALK.—There are some interesting points connected with the elimination of chloride of sodium during this period. The nitrogenous food, which contained nearly all the chloride of sodium, was diminished by 31 per cent., and the average quantity of salt used as a condiment was 35 grains (2.265 grammes). The average elimination of chloride of sodium by the kidneys was only 65.08 grains (4.217 grammes); but a large quantity must have been eliminated by the skin, the average cutaneous and pulmonary exhalation daily being 138.41 oz. (3,875.18 grammes), against 61.63 oz. (1,690.91 grammes) for the five days before the walk, and 62.82 oz. (1,706.78 grammes) for the five days after the walk.

On the third day, when the food contained probably the minimum proportion of salt, the salt of the urine was reduced to 44.45 grains (2.88 grammes), about 32 per cent. below the average for the five days. On the fourth day it is probable that a little more salt was taken with the food. On this day the exercise was fifty-seven miles; but it was on this day that Weston broke down and was forced to take a long rest. The chloride of sodium for this day was reduced to 28.78 grains (1.865 gramme), nearly 56 per cent. below the average. On the next day, when reaction took place, the salt returned to about the average. In view of the disappearance of the chloride of sodium of the

urine in certain febrile conditions, this diminution in its quantity on the day of great constitutional depression is interesting, although its exact significance is not apparent.

THIRD PERIOD, FIVE DAYS AFTER THE WALK.—The variations in the chloride of sodium of the urine during this period were very great. The smallest quantity was on the first day, when it was 66.41 grains (4.303 grammes). The largest quantity was on the third day, when it was 622.58 grains (40.338 grammes). The quantity of urine on this day was 84.18 fl $\bar{3}$ (2,490 cc.). I could not connect these variations either with the diet or with the salt used as a condiment, which was weighed each day and varied considerably. The only point connected with the daily variations during this period is the small quantity on the day next after the walk, when it was only 66.41 grains (4.303 grammes), while the salt actually used as a condiment on that day was 65.62 grains (4.252 grammes).

The average daily quantity of chloride of sodium of the urine for this period was 312.40 grains (20.241 grammes). The nitrogenous food was increased by 30 per cent. over the average for the five days before the walk. The average quantity of salt used as a condiment was 42 grains (2.721 grammes), an increase of nearly 22 per cent. over the average for the five days before the walk.

AVERAGES FOR THE THREE PERIODS.—The averages for the three periods of five days each are as follows:

First period, five days before the walk, 159.45 grains (10.331 grammes).

Second period, five days of the walk, 65.08 grains (4.217 grammes).

Third period, five days after the walk, 312.40 grains (20.241 grammes).

These averages show a great diminution in the chloride of sodium of the urine during the walk, due in a great measure, undoubtedly, to a diminution in the quantity of salt ingested. In the absence of exact estimates of the quantity of salt introduced, it is impossible to state definitely the influence of exercise on its elimination by the kidneys. Probably it is diminished, a much larger quantity than usual being eliminated by the skin. An argument in favor of this view is the small quantity in the urine the

day next after the walk, when a large quantity was introduced with the food.

The only explanation I can offer of the great increase in the chloride of sodium during the five days after the walk is in the larger quantity taken with the food, and possibly the cessation of the influences which diminished it in the urine during the five days of the walk.

ABNORMAL MATTERS IN THE URINE

There is very little to be said in regard to the abnormal matters discovered by microscopical examination of the urinary sediments. During the first period, five days before the walk, there was a constant deposit of octahedra of oxalate of lime. During the second period, five days of the walk, oxalate of lime was found daily. On the fifth day of this period, in addition to oxalate of lime, there was a small quantity of the amorphous phosphates. The oxalate of lime continued during the third period, five days after the walk, with the exception of the fourth day, when there were no abnormal matters. On the first day of this period the sediment contained, in addition to oxalate of lime, amorphous urates in small quantity. On the second and the third day of this period, in addition to oxalate of lime, the sediment contained crystals of uric acid. On these days the quantity of uric acid in the urine, determined by analysis, was very small, and the crystals were probably due to increased acidity of the urine. I can offer no explanation of the presence of any of these crystals in the urine nor can I connect them with any of the conditions observed.

On the second and the third day of the third period, five days after the walk, the urine contained a trace of sugar. There was no increase in the quantities of starchy and saccharine matters in the food on these days to account for the sugar, the presence of which can not readily be explained.

In conclusion, it is evident, from the results of these investigations, that the question of the influence of muscular exercise upon the elimination of nitrogen can be accurately studied only by comparing the nitrogen of the food with the nitrogen of the excretions; and this should be done

if possible upon a perfectly physiological diet. It is indispensable, also, to extend the experiments over periods of several days each; otherwise the results will necessarily be confused and unsatisfactory. The observations in regard to the body-weight and various other conditions were necessary to control the more important points to be considered. The great amount of material collected and its analysis and tabulation have involved considerable labor, which, however, has been rewarded by important conclusions of a definite and positive character.

At the risk of presenting to the reader an unattractive mass of statistics, I have thought it proper to publish, not only the general facts and deductions, but the exact data collected, arranged in a form that may be useful to other investigators. I feel confident that I shall not be reproached for tediousness of detail by those who are interested in the important physiological questions involved, particularly those who have carefully studied the literature of these questions for the past few years.

XX

SUPPLEMENTARY REMARKS "ON THE EFFECTS OF SEVERE AND PROTRACTED MUSCULAR EXERCISE; WITH SPECIAL REFERENCE TO ITS INFLUENCE ON THE EXCRETION OF NITROGEN"

Published in the "Journal of Anatomy and Physiology," Cambridge and London, for October, 1876.

IN June, 1871 I published in the "New York Medical Journal" an account of a series of observations made upon Weston, the pedestrian, during one of his feats of endurance. My researches have lately been in part repeated and confirmed in England by Dr. Pavy. My original observations were made with the utmost care, and they involved a great deal of labor. They were most decidedly opposed, in their results, to the modern view regarding the influence of muscular exercise on the excretion of urea, which is based upon the experiments of Fick and Wislicenus, made in 1866, and upon other observations apparently confirmatory of the notion that the elimination of urea is not increased by muscular work. This view I believe to be incorrect; and I regard the experiments upon which it rests as imperfect, faulty and made under unphysiological conditions.

The question of the influence of muscular exercise on the elimination of nitrogen being of great importance in its pathological as well as in its physiological relations, it was to be expected that conclusions opposed to the generally-accepted ideas, even when deduced from very extended experiments, would be viewed with distrust and receive adverse criticism. I have not failed to realize this expectation; although it seemed to me that my conclusions could not be successfully controverted with-

out a denial of the accuracy of my experimental data. I shall here refer only to the criticisms of Dr. Pavy, as he is now the one physiologist who is in a position to judge, from his own knowledge, of the reliability of my observations. These criticisms, however, seem to me to be general rather than definite and positive. They are summed up substantially in the following paragraph, quoted from Dr. Pavy's work on "Food and Dietetics":—

"Now, apart from the fact that a marked deviation from the physiological state existed when the results upon which the conclusions are based were yielded, is there anything in the results to show that in reality we have more to deal with than simply a consumption of nitrogenous material within the system beyond the supply for the time from without? Taking the figures throughout, there is not much more to be seen than a difference occasioned by a falling off in the amount of nitrogen ingested during the first four days of the walk; and it is well known that when the ingesta do not furnish what is wanted for meeting the expenditure going on (as during inanition), the resources of the body are drawn upon, and the nitrogenous matter existing in the various parts—both solids and fluids—wastes or yields itself up as well as the rest. On the fifth day, after a prolonged sleep, which appears to have restored the flagging powers, the previous relation was reversed. The food ingested afforded more than enough to meet the requirements. There was a gain of $1\frac{1}{2}$ pound in body-weight, and according to the figures, the nitrogen discharged fell short by 50.27 grains of that which entered, notwithstanding a walk of forty miles and a half was performed." *

This paragraph, without a knowledge of the details of my experiments, may seem obscure. I think Dr. Pavy intended to reason as follows:—Although I had demonstrated, for the first four days of a feat performed by Weston in which he had walked, the first day 80 miles, the second day 48 miles, the third day 92 miles and the fourth day 57 miles, that there was a large increase in the nitrogen excreted over the nitrogen of food, it is assumed by Dr. Pavy that this apparent excess was due to a deficient ingestion of nitrogen and not necessarily to an increase in the excretion of nitrogen. The fact is that comparing four days, during which 277 miles were walked, with four days before, during which 26 miles were walked, in four days,

* Pavy, "Food and Dietetics," Philadelphia, 1874, p. 71.

walking 26 miles, there were 1,336.06 grains of nitrogen in the food, against 790.78 grains during four days, walking 277 miles, or a deficiency in the nitrogen of food during the latter period of 545.28 grains. During the four days, walking 26 miles, the nitrogen excreted was 1,252.17 grains, against 1,473.85 grains during the four days, walking 277 miles, or an excess of nitrogen excreted of 221.68 grains. It is evident that the excessive exertion of walking 277 miles in four consecutive days induced an increase in the excretion of nitrogen; not only sufficient to equal the deficiency of the nitrogen of food, but a considerable excess. The excess of the nitrogen excreted during the four days, walking 277 miles, over the four days, walking 26 miles, irrespective of the nitrogen ingested, was 221.68 grains; and the excess of nitrogen excreted during the four days, walking 277 miles, over the nitrogen ingested during the four days, walking 26 miles, was 137.79 grains. It seems to me that the figures and deductions which I gave in my original article, in which I show the effects of prolonged and severe muscular exercise on the excretion of nitrogen, not only in absolute quantity but in proportion to the nitrogen ingested, are sufficiently clear and distinct; and the complications in these deductions, if they exist, are due to the process of reasoning from my figures employed by Dr. Pavy. It does not appear that any physiological demonstration could be more positive than that of the proposition that muscular exercise increases, not only the absolute quantity of nitrogen excreted, but the proportionate quantity of nitrogen eliminated to the nitrogen of food.

My first impression, in studying the experiments of Fick and Wislicenus, was that the observations on the influence of exercise upon the elimination of nitrogen were made upon a purely non-nitrogenous diet on account of the labor and difficulty attending an accurate estimation of the nitrogen of food; but it now seems to me that this was not the only idea under which this method of experimentation was adopted. It is a seductive, and was a more or less novel idea, that the animal organism, after it has become fully developed, is a machine which consumes food as fuel, and that it does not constantly wear out its own substance by work and repair itself by the ingesta. With this view, it

would seem possible to reduce the values of food to mathematical accuracy, calculating the heat-units, foot-pounds, etc., of various articles of diet. Such calculations would be very indefinite for any restricted period of time, adopting the view that the nitrogenous constituents of the body wear and are consumed with muscular work and that they are regenerated by the nitrogenous matters of food. A necessary basis for an accurate estimation of heat and work-units of food is the idea that food is directly consumed in the production of heat and in work. While calculations of these units with mathematical accuracy would be very desirable as giving definite form to ideas of the value of food, they still want a positive basis in fact. In carrying out this idea, it seems to me that the value of many of the experiments is made to depend on the assumption of the truth of the proposition which they are intended to support.

In view of the importance of the results obtained by me, and, as I believe, confirmed by the recent observations of Dr. Pavy, it would be interesting to assimilate and compare the two sets of observations, the more so as I could scarcely have hoped that independent researches would have been made under the same unusual conditions; viz., the same subject undertaking a similar feat of endurance. In the account published by Dr. Pavy thus far I do not find any reference to the results obtained by me in 1870 and published in 1871. If I should not be anticipated by Dr. Pavy, I shall be interested to place the figures of the two series of observations side by side; but I hope that Dr. Pavy, who is now fully prepared to criticise my results, will give them the study and attention that he bestowed upon them when he had had no opportunity to personally test their accuracy. In the calculations which I made of the quantities of nitrogen of food I used the same estimates for all the three periods, before, during and after the walk. If any errors existed in these estimates, such errors would have equal value in the different periods and would not materially change the comparative results. It would be interesting to use these same estimates in calculating the nitrogen of the food taken while Weston was under the observation of Dr. Pavy.

CORRECTIONS IN THE TABLES PUBLISHED IN 1871*

In calculating the proportion of nitrogen excreted to the nitrogen of food, I fell into an error sufficiently serious to demand correction, although it does not affect the general conclusions deduced from my observations. I first calculated the quantity of nitrogen excreted for every hundred parts of nitrogen of food, for each day, by multiplying the nitrogen excreted by 100 and dividing by the nitrogen of food, which gave correct results; but in calculating the average proportions of nitrogen excreted for the five days before the walk, five days of the walk and five days after the walk, I added for each period the proportionate excretion of nitrogen for the five days and obtained the average by dividing by five. This was an error, as I was using relative and not absolute quantities. I fell into this error simply because the process was a little easier than to divide the average amount of nitrogen excreted for the five days by the average amount of nitrogen ingested for the same period.

* The corrections in the tables—which followed in this article as originally published—have been made in Article XIX., as republished here.

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